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1. Johnson DAW and Malik NA; Acta Psychiat Scand 1975; *51*: 257-267.
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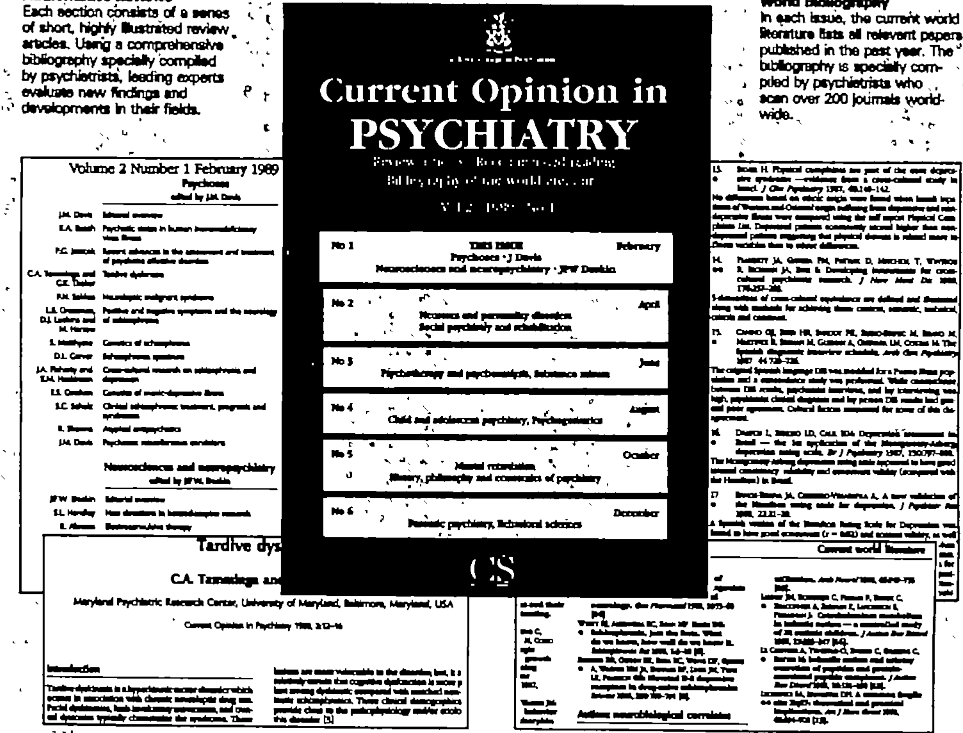

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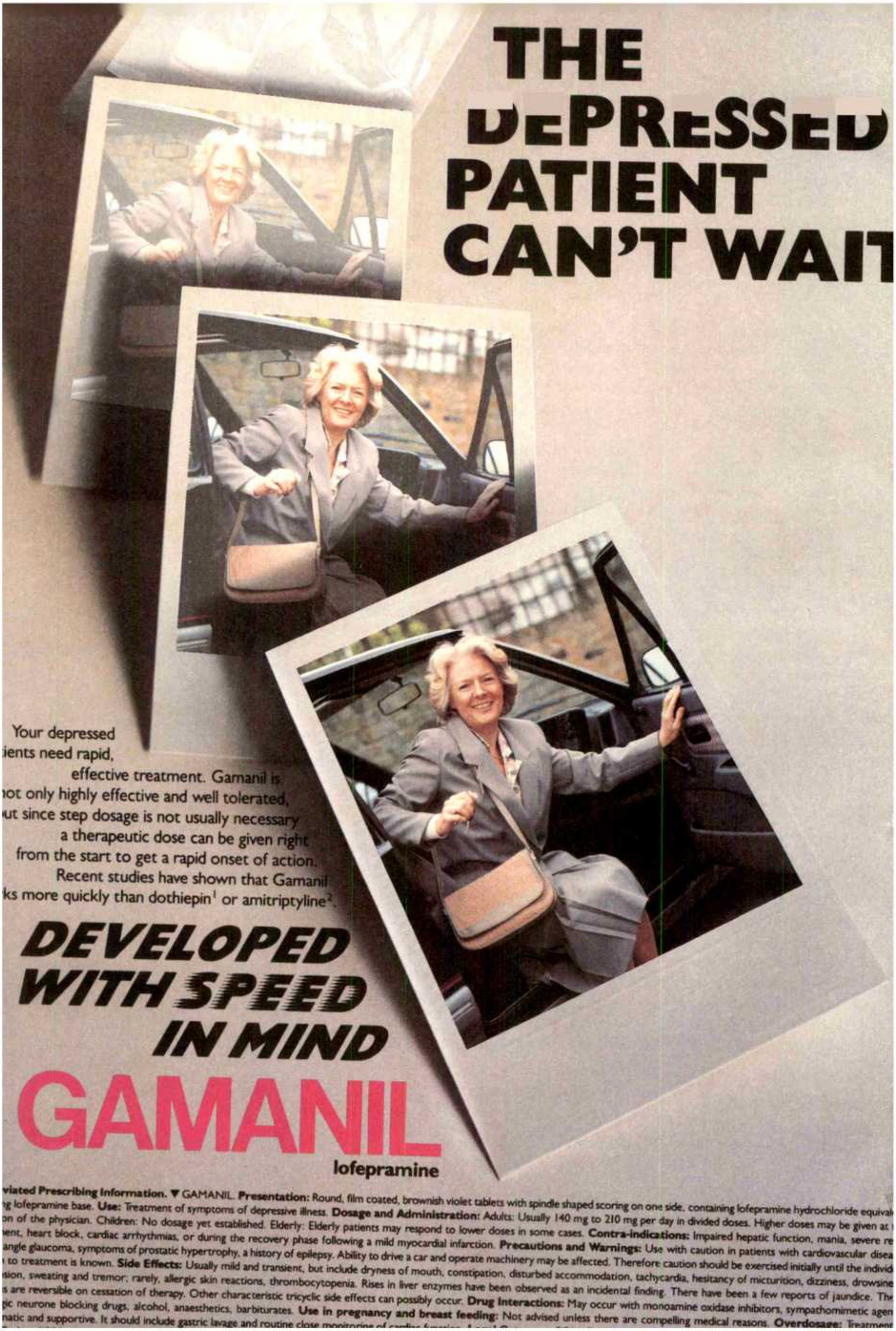

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British Journal of Psychiatry (1989), 155, 1–11 **Lecture**

Neuronal Lipopigment: a Marker for Cognitive Impairment and Long-Term Effects of Psychotropic Drugs*

J. H. DOWSON

Lipopigment, identifiable in the fluorescence microscope, is thought to be cellular debris partly derived from free-radical-induced peroxidation of cellular constituents. The volume of neuronal lipopigment has been positively correlated with advancing age, Alzheimer dementia, and the neuronal ceroidoses, while various changes in neuronal lipopigment have been reported in association with the chronic administration of dihydroergotoxine, ethanol, phenytoin, centrophenoxine, and chlorpromazine. An increase in the volume of neuronal lipopigment may indicate increased functional activity of the cell, impaired removal of pigment or anoxia. Chronic administration of agents which can be correlated with decreased neuronal lipopigment in animal models might protect neuronal function against any adverse effects associated with (but not necessarily resulting from) lipopigment accumulation in normal ageing, anoxia, or certain degenerative diseases. Long-term studies of the prophylactic use of such agents, or of drugs which neutralise free radicals, may be indicated. Other clinical applications of such drugs may include protection against the effects of free radicals formed during periods of oxygen deprivation.

A tissue pigment is a substance which has a naturally distinctive colour, and so-called lipopigment consists of discrete or aggregated particles which appear yellow or brown in unstained tissue sections. Lipopigment is present in many organs and cell types, including neurones. Although it can be demonstrated by various staining techniques, it exhibits a striking yellow fluorescence in unstained tissue, so that fluorescence microscopy has proved useful for its identification and examination (Dowson & Harris, 1981).

Fluorescence occurs when certain substances emit light whose wavelength is longer than that of the exciting light, and lipopigment can be defined operationally as a tissue pigment which emits yellow fluorescence when irradiated by ultraviolet or blue light.

In the last century it was noted that while the cell bodies of neurones in elderly individuals were often almost filled with lipopigment, this was not the case in the foetal brain, and the gradual accumulation of neuronal lipopigment has been considered to be one of the most consistent correlates of ageing in the mammalian nervous system. Most lipopigment in neurones is found in the cell body, but pigment particles can also be present in axons and dendrites. There are considerable variations in the characteristics of lipopigment between neurones; for example, in respect of the size, number and distribution of particles, their fluorescent characteristics, and their composition. Also, the rate of accumulation of intraneuronal lipopigment varies between neuronal groups. Such variations in lipopigment characteristics can be used to identify groups of neurones which share particular functions.

Because of the variations in its properties, lipopigment should be considered as an umbrella term for a variety of related pigments, and there are two main subcategories, *lipofuscin*, which accumulates during normal ageing, and *ceroid*. The latter is not a normal cerebral constituent and indicates a pathological process. However, each of these major subcategories is not homogeneous (Dowson, 1982*a*).

There is evidence that lipopigment contains debris derived from cell damage and from the normal processes of renewal of cellular constituents such as membranes, mitochondria and lysosomes. It is believed that the reaction of unstable 'free radicals' (which have an odd number of electrons) with such constituents, in a process of lipid peroxidation, contributes to the formation of lipopigment (Halliwell & Gutteridge, 1984). Lipopigment is, therefore, usually considered as cellular debris, and it has been claimed that there may be a constant turnover of lipopigment, due to the extrusion of fragmented pigment particles or some constituents of lipopigment through the cell membrane. These may eventually enter a capillary lumen via glial cells (Glees & Spoerri, 1975). However, it is not certain that routine removal of intraneuronal lipopigment (or of certain constituents of lipopigment) takes place to a significant extent, and opinion also varies as to whether or not neuronal lipopigment in ageing or disease is harmful. Although ageing is associated with a reduced number of neurones and an impaired functional capacity of remaining neurones with changes in, and loss of, synapses (Glick & Bondareff, 1979), together with reduced RNA synthesis, there is no clear evidence that lipopigment accumulation is a causal factor (Mann *et al*, 1978). But this is possible, and mechanisms for an adverse effect of lipopigment on neuronal function could include a toxic effect of the pigment or of other end products of lipid peroxidation (McBrian & Slater, 1982), the displacement of organelles, and the disruption of intracellular transport in the cell body or in the cell processes. Any adverse effect of lipopigment may vary between different neuronal groups and interact with other factors; however, it seems clear that massive accumulations of intraneuronal lipopigment need not have a clinically significant effect on neuronal functions, as, for example, olivary neurones in elderly individuals with no known disease or neurological impairment are almost filled with lipopigment. Nevertheless, lipopigment accumulation may have subtle effects on cerebral function and make a significant contribution to the functional decline of ageing neurones. If so, the sequelae of lipopigment accumulation in cell processes may be important, despite the concentration of lipopigment in the cell body.

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*Based on a Maudsley Bequest Lecture at the Royal College of Psychiatrists Winter Quarterly Meeting, 28 January 1987.

It has even been suggested that lipopigment can act as a reservoir of oxygen in conditions of hypoxia (Karnaukhov, 1972) but there is no convincing evidence for such a beneficial role.

Correlates of changes in neuronal lipopigment

Various factors have been claimed to be associated with changes in lipopigment, in particular the estimated volume of lipopigment in the neuronal body.

In addition to advancing age, the reported correlates of increased volume of neuronal lipopigment are Alzheimer dementia, the neuronal ceroidoses (ceroid-lipofusinoses), the chronic administration of ethanol, phenytoin or dihydro-ergotoxine (Hydergine, Sandoz), and increased neuronal activity. While it should be noted that a diet deficient in vitamin E has been reported to result in increased lipopigment deposits in the retinal pigment epithelium in animal studies, an increase was not found in the two neuronal groups which were also examined (Katz *et al*, 1984).

A decrease in the volume of neuronal lipopigment has been correlated with decreased neuronal activity or chronic administration of any of the following: centrophenoxine (meclofenoxate), chlorpromazine, vitamin E supplements (Rudra *et al*, 1975; Freund, 1979), acetylhomocysteine thiolactone (Totaro *et al* 1985), or butylated hydroxytoluene. Constantinides *et al* (1986) examined the effects on the spinal-cord neurones of mice of chronic administration of the natural antioxidant vitamin E or the synthetic antioxidant butylated hydroxytoluene over eight months, and reported that both these regimes were associated with a reduced accumulation of neuronal lipopigment. These authors speculated that the chronic administration of antioxidants might have therapeutic applications in clinical practice, but pointed out that relatively large doses would probably be necessary to achieve even a modest suppression of lipopigment accumulation. These data suggested that humans would have to consume at least 10 g/day of vitamin E. Modification to the blood/brain barrier for antioxidants, new antioxidants or mutually potentiating combinations might conceivably enable smaller antioxidant doses to effect a detectable diminution in lipopigment accumulation.

Of particular interest to psychologists and psychiatrists is evidence which suggests that increased functional activity in neurones may be associated with increased lipopigment accumulation, and vice versa. Indeed, lipopigment can be considered as the only currently detectable histological remnant of previous mental activity. Scholtz & Brown (1978) examined the lateral geniculate bodies of a series of normal and blind patients and claimed that the amount of neuronal lipopigment was less in the blind patients than in the controls, although this had not been the finding of Brizzee *et al* (1975) in their studies on rhesus monkeys. Further evidence that neuronal activity is related to lipopigment accumulation was obtained by comparing hibernating and non-hibernating hamsters (Papafrangos & Lyman, 1982): animals that hibernated lived longer and the findings indicated a slower rate of lipopigment accumulation in both heart and brain. However, it appeared that the total amount of accumulated lipopigment during the life-span did not differ between the two groups. The effects of psychologically determined neuronal activity have also been reported to be associated with differences in neuronal lipopigment accumulation. Kerenyi *et al* (1986) subjected rats to a "repeated conflict of the feeding and defensive reflexes" over a period of six months, and it was claimed that this correlated with a marked increase in the volume of lipopigment in Purkinje cells. However, many variables, such as diet and activity, were uncontrolled, and the lipopigment was only quantified by visual estimates. Nevertheless, the effects of psychological stress deserve further study. Basson *et al* (1982), in their study of the effects of a daily 'training programme' involving treadmill exercise on rats, for periods up to 17 months, claimed that brain lipopigment was increased, although this involved the analysis of tissue homogenates.

The correlates of changes in neuronal lipopigment which are of more immediate relevance to psychiatry are ageing, certain diseases, and various drugs (including ethanol). These will now be considered in more detail, illustrated by data derived from fluorescence microscopy.

Techniques of fluorescence microscopy

The light source for the fluorescence microscope is a mercury arc lamp, and blue light is reflected onto the mounted tissue section from above by a special (dichroic) mirror which, while reflecting the blue light down onto the specimen, allows the upward transmission of the resulting yellow fluorescence. Additional barrier filters placed in the light path between the mirror and the observer can restrict transmission of the yellow fluorescence to specified wavelength bands (Dowson & Harris, 1981).

The yellow lipopigment fluorescence can be recorded in three ways: firstly, a photograph can be taken; secondly, the intensity of the yellow fluorescence from an individual cell body can be measured, which is a method for quantifying lipopigment that is indicated for large aggregations of particles; and, thirdly, the intensity of a series of narrow bands of the fluorescence spectrum can be measured. These give the 'emission spectrum' of the pigment in the region under investigation. As emission spectra reflect the composition of the pigment, and can vary in relation to many factors including age, type of neurone and disease, lipopigment emission spectra can be an important source of information (Dowson, 1982*a*).

Neuronal lipopigment in relation to cognitive impairment

In certain neuronal groups, the volume of intraneuronal lipopigment has been positively correlated with advancing age, Alzheimer dementia and the neuronal ceroidoses, all of which can be associated with cognitive impairment.

Neuronal lipopigment in ageing and Alzheimer dementia

In man, approximately linear rates of increase of neuronal lipopigment in ageing have been reported in the inferior olivary nucleus, dentate nucleus, pyramidal cells of the hippocampus and Purkinje cells (Mann & Yates, 1974; Mann *et al*, 1978). Also, the rate of increase of neuronal lipopigment has been correlated with the rate of reduction of cytoplasmic RNA in olivary neurones and anterior horn cells of the spinal cord. It has been suggested that there is a threshold volume of lipopigment, above which further increases may be causally related to a more rapid rate of reduction of cytoplasmic RNA, such as was reported in the olivary neurones in the eighth and ninth decades (Mann & Yates, 1974). (Reduced RNA may be associated with impaired functional activity.) However, another study has reported that the rate of decrease in cytoplasmic RNA, and also in nucleolar volume, is similar in Purkinje cells, neurones of the dentate nucleus and in pyramidal cells of the hippocampus, despite the different rates of lipopigment accumulation in these three cell populations (Mann *et al*, 1978).

It has been claimed that variations in the volume of neuronal lipopigment are correlated with the neuronal ceroidoses, progeria, Jakob–Creutzfeldt dementia, Huntington's chorea and Alzheimer dementia (Brizzee, 1975; Brizzee *et al*, 1975; West, 1979). Several studies have reported that Alzheimer dementia is associated with increased lipopigment in various populations of neurones, including spinal cord neurones (Malamud, 1972; Kent, 1976; Yamada, 1978), although it has also been claimed that there are no increases (Mann *et al*, 1977; Mann & Sinclair, 1978; Scholtz & Brown, 1978). Mann & Sinclair (1978) claimed that although Alzheimer dementia was associated with decreased amounts of intraneuronal cytoplasmic RNA, together with reduced nucleolar volume, in Purkinje cells, dentate nucleus, hippocampus and inferior olivary nucleus, there was no increase in neuronal lipopigment in Alzheimer dementia in any of these cell populations. These studies employed various methods to quantify neuronal lipopigment, including estimation by eye, counting grid intersections overlying lipopigment, and measuring the intensity of lipopigment autofluorescence, all of which present complex methodological problems.

Dowson (1982*b*) reported data derived from a method for measuring the intensity of neuronal lipopigment fluorescence which was used to estimate the volume of neuronal lipopigment in layer III of a region of the parietal cortex and in the inferior olivary nucleus from post-mortem tissue affected by Alzheimer dementia and in specimens from non-demented controls. The results indicated a linear relationship between the accumulation of neuronal lipopigment and advancing age, in both neuronal populations of the non-demented group and in the olivary neurones of the demented group. However, in the demented group, the estimated neuronal lipopigment volume in the parietal neurones was not significantly correlated with age, and the estimated neuronal lipopigment volume in the olivary neurones was significantly increased, when age had been taken into account.

In the so-called 'normal' elderly, there have been many reports of cerebral changes, such as cortical atrophy, synaptic changes, loss of dendrites, and a reduced number of cells in various neuronal populations (Earnest *et al*, 1979; Brizzee & Knox, 1980). However, in the case of the inferior olivary nucleus, the evidence of loss of neurones with ageing is conflicting: one study of 18 subjects up to age 89 did not find a decreasing number of neurones with increasing age (Monagle & Brody, 1974), while Sandoz & Meier-Ruge (1977) reported a 20% decrease in the number of olivary neurones between the ages of 20 and 80. However, whatever the degree of neuronal loss in a particular neuronal population, it is possible that the accumulation of neuronal lipopigment is a contributory factor to functional impairment and cell death in various neuronal populations, in the normal ageing process.

The finding of increased lipopigment in the olivary neurones in Alzheimer dementia (Dowson, 1982*b*) was consistent with a previous report of a greater reduction of cytoplasmic RNA and of nucleolar volume in olivary neurones in Alzheimer dementia, and it is possible that an increase in neuronal lipopigment has a pathogenic effect on various neuronal populations in this disease. Although the amount of lipopigment in the parietal neurones in the demented group was not significantly different from that of the non-demented group, this study found that, at the terminal stage of dementia, a linear relationship between lipopigment accumulation and ageing had been destroyed by the disease process. It is possible that, in the earlier stages of dementia, lipopigment is also increased in many neurones in the cerebral cortex which disappear before death and that this may be a secondary contributory factor in the development of impaired neuronal function. The critical threshold, above which an increase in lipopigment is harmful, may vary between cell groups and may also depend on any concomitant disease process. Thus, in Alzheimer dementia, the effects of relatively modest accumulations of neuronal lipopigment may summate with those of other pathogenic mechanisms. In view of the possible pathogenic effects of neuronal lipopigment, both in cell bodies and cell processes, research into factors which reduce the rate of lipopigment formation, or the amount of lipopigment which has already accumulated, may eventually provide a means of reducing the effects of one possible contributory factor to the development of cognitive deficits in both normal ageing and Alzheimer dementia. Even if lipopigment is not harmful, if its accumulation reflects cellular damage, factors which reduce its accumulation may have a beneficial effect on cerebral function by reducing the adverse effects of pathogenic mechanisms.

Neuronal lipopigment in the neuronal ceroidoses

The neuronal ceroidoses (ceroid-lipofuscinoses) are characterised by abnormally excessive amounts of neuronal lipopigment, although other types of cell are also affected (Zeman, 1976). The clinically heterogeneous ceroidoses are usually characterised by progressive blindness and neurological deficits, including dementia, and have been variously classified on the basis of age of onset, age at death, clinical presentation, and pathological findings. Most occur in children but some present as a dementia in adult life, when they are known as Kufs' disease, although the adult-onset cases show considerable variation in respect of family history, age of onset, presenting symptoms, clinical features, duration of illness, and pathological findings (Zeman & Hoffman, 1962; Pallis *et al*, 1967; Chou & Thompson, 1970; Boehme *et al*, 1971; Kornfeld, 1972; Dom *et al*, 1979; Badurska *et al*, 1981). Such heterogenicity may indicate that adult-onset neuronal ceroidosis consists of several distinct disorders, and as the age of onset can be uncertain, some cases with an apparent adult onset may be protracted forms of childhood disorders; a protracted form of juvenile neuronal ceroidosis has been described (Goebel *et al*, 1976). Also it should be noted that adult gangliosidoses have been reported (Rapin *et al*, 1976; Suzuki *et al*, 1979), and although the gangliosidoses have been differentiated from the ceroidoses on several grounds, including the lack of fluorescence of the neuronal granular accumulations in these disorders (Hittner & Zeller, 1975), a case of a gangliosidosis, which was diagnosed by an absence of B-galactosidase activity in leukocytes and fibroblasts, was associated with strongly fluorescent neuronal granular inclusions (Lowden *et al*, 1981). In addition, a case of mucopolysaccharidosis, Sanfilippo's syndrome, in which urinary analysis showed a high content of heparan sulphate, showed strongly fluorescent neuronal accumulations (Oldfors & Sourander, 1981).

The characteristics of the shape of the emission spectra of the fluorescence derived from regions of lipopigment can be used to distinguish lipofuscin, which accumulates in healthy brains during ageing, from ceroid in the neuronal ceroidoses. Although differences in the emitted fluorescence can often be detected by observation of variations in the colour of the yellow fluorescence, such differences can be reliably quantified by calculation of a ratio between different points on the spectrum. By use of this technique the statistical significance of differences between the pigments in normal ageing, the ceroidoses and other disorders can be readily demonstrated.

Dowson (1983) reported characteristics of neuronal lipopigment fluorescence spectra from a case of adult-onset neuronal ceroidosis and compared these with spectra from 14 brains which were unaffected by neurological disease. The results were also compared with emission spectra from childhood-onset ceroidoses (Batten's disease) and animal ceroidoses which had been previously reported (Dowson *et al*, 1982).

Post-mortem tissue was examined from a female patient with adult-onset neuronal ceroidosis. Her husband had first noticed a change in behaviour when she was aged 34. She had gradually lost interest in running her home and looking after her children, and this was followed by a gradual deterioration over the subsequent seven years, which involved irritability, difficulty in pronouncing words and a dragging of the left leg. In the final year of life she was unable to dress herself and exhibited a severe dementia. Six months prior to death she was able to give her name and knew she was in hospital, but she had a non-fluent dysphasia with occasional pallilalia and echolalia. She estimated the duration of the interview as 5 minutes after both 5 and 30 minutes. She was unable to repeat a name and address and could not draw or copy a cube. Power and tone in the limbs was normal, and although her motor behaviour was jerky, there were no abnormal movements at rest. Computerised tomography showed that while ventricular size was within normal limits, there was apparent cerebral atrophy with widening of the inter-hemispheric fissure and cerebral sulci.

The majority of larger neurones in the frontal and parietal cortex exhibited distended cell bodies containing marked accumulations of lipopigment, and many neurones, particularly in the frontal cortex, had a lipopigment-filled appendage, similar to the 'giant axonal dilatations' described in childhood-onset ceroidoses (Braak & Goebel, 1979). The bodies of the Purkinje cells also showed an increased accumulation of lipopigment.

The emission spectra derived from these abnormal lipopigment accumulations could be distinguished from the spectra from lipofuscin in non-diseased brains, and from ceroid in the childhood-onset ceroidoses. The characteristics of an emission spectrum probably reflect the composition of the lipopigment, and spectral analysis may aid the identification of different pathogenic mechanisms which underlie the various types of neuronal ceroidosis. This technique has been used for the diagnosis of Kufs' disease in brain biopsies from dementias of uncertain aetiology.

Neuronal lipopigment in relation to psychotropic drugs

The following psychotropic agents have been claimed to produce changes in neuronal lipopigment: dihydroergotoxine, centrophenoxine, chlorpromazine, phenytoin and ethanol. Chronic administration of agents which are correlated with decreased neuronal lipopigment might conceivably protect cerebral function against any adverse effects of lipopigment accumulation or of pathogenic mechanisms leading to lipopigment accumulation, while an increase in neuronal lipopigment may indicate increased functional activity of neurones or a toxic effect of a drug. Thus, the examination of neuronal lipopigment in animal models has varied potential in pharmacological research (Johnson *et al*, 1986).

Dihydroergotoxine

Dihydroergotoxine is the most extensively studied of all the drugs which have been used in attempts to alleviate chronic cognitive impairment in the elderly. Yesavage *et al* (1979) reviewed 33 clinical studies of dihydroergotoxine, of which 22 were considered to be well-designed controlled trials. All these 22 studies reported significant improvement in some behavioural or psychological measure, and in 18 of these the improvement was considered to be of practical benefit. Studies which employed the highest doses, up to 4.5 mg/day, claimed the best results. McDonald (1969), in another review of 26 studies, concluded that 13 symptoms, involving cognitive dysfunction, depression and behaviour, were significantly improved in about half the studies.

Huber *et al* (1986) have reported results after five years of a placebo-controlled long-term study to assess the preventative effects of dihydroergotoxine (4.5 mg daily) on medical, psychological and electrophysiological variables in healthy, elderly volunteers. Although statistical analysis of the data did not yield significant differences, the authors claimed that the pattern of several trends suggested that the drug regime did have a positive effect in maintaining physical and mental health.

There are a variety of reports of the pharmacological effects of dihydroergotoxine, including a claim that it can minimise the harmful effects of cerebral anoxia (Paoiorek & Wyllie, 1980). However, the effects of dihydroergotoxine on neuronal lipopigment have received little attention. Nandy & Schneider (1978) claimed that this drug was correlated with reduced lipopigment accumulation in cultured mouse neuroblastoma cells, while Dowson (1985) found that daily (5 days per week) injection of dihydroergotoxine to rats over a period of 12 weeks was associated with a significant increase in mean area overlying neuronal lipopigment in the CA3a region of the hippocampus. This suggested that chronic dihydroergotoxine administration was associated with an increased volume of lipopigment in these neurones. It is possible that the drug stimulates neuronal metabolism which leads to increased lipopigment accumulation, or the result may indicate drug toxicity. Further studies on the effects of dihydroergotoxine on lipopigment may help to determine the effects of long-term administration at various dose levels on neuronal structures.

Centrophenoxine

The clinical use of centrophenoxine has been advocated for various forms of dementia, cerebrovascular accidents and head injuries, although the clinical literature is sparse. One of the reported effects of this drug is to protect animals against the effects of cerebral anoxia or cyanide administration (Miyazaki *et al*, 1976), which may be related to an enhanced activity of the pentose phosphate pathway. This suggests that centrophenoxine may be of value in some cases of cerebrovascular accident or arteriosclerotic dementia, in other pathological states in which there is reduced cerebral oxygenation, or in other conditions where there is tissue-oxygen lack such as angina or intermittent claudication. However, there is no reliable information of the use of this drug in these disorders.

Many of the published clinical studies of centrophenoxine were not controlled and involved diagnostically heterogeneous groups of elderly individuals. However, there have been four double-blind controlled studies. Oliver & Restell (1967) tested various functions which included digit span, counting backwards, continuous subtraction in steps of 3, and the ability to retrieve remote memories, in patients with evidence of memory impairment. No significant effect of centrophenoxine was detected, but this study did not investigate the process of learning new material. However, Gedye *et al* (1972) reported that administration of the drug to patients showing clinical evidence of a mild to moderate degree of either Alzheimer or arteriosclerotic dementia led to a statistically significant improvement in the performance of a task involving new learning. Patients were recruited from in-patient geriatric units and 15 pairs of subjects were matched. Centrophenoxine, 600 mg twice daily, or a placebo, was allocated randomly within each pair and treatment was continued for six weeks. The third study, by Marcer & Hopkins (1977), examined the effects of centrophenoxine on memory for new information in normal elderly volunteers who were recruited from general practice. Thirty-one subjects received the drug and 29 received placebo. The trial was double-blind, the dose was 600 mg twice daily for 6 months, and the subjects were tested at 0, 3, 6, and 9 months. As in Oliver & Restell's study, administration of the drug did not correlate with an improvement in remote memory functions or immediate memory as measured by digit-span testing; however, as in the study of Gedye *et al*, there was a significant improvement in memory for new information, and in this study this was measured by a delayed free-recall test. (Subjects listened to a list of ten words which were repeated until seven could be immediately recalled; recall was then retested after an interval of about 30 minutes.) Also, several patients who were receiving the drug reported a feeling of well-being and increased alertness.

The most recent study on the effects of centrophenoxine, by Harris & Dowson (1986), examined the effects of the drug, 600 mg twice daily for 12 weeks, on 20 residents in homes for the elderly who exhibited mild to moderate memory impairment which was probably due to senile dementia of the Alzheimer type. Initial referral was from the officers in charge of the homes, who were asked to nominate residents who had been considered to show persistent memory disorder for at least six months. Residents were then excluded if it was judged that impaired cognitive function was probably due to factors other than a gradually progressive disorder compatible with a diagnosis of senile dementia of the Alzheimer type. The testing procedures included a digit-span test, a short questionnaire for temporal orientation and memory for remote events, the Digit Symbol test of the Wechsler Adult Intelligence Scale (Wechsler, 1958), a paired-associate learning test and the recall of a ten-word list. Each subject was scheduled to receive periods of placebo and of centrophenoxine, in a randomly-determined order, and nine of the 20 subjects completed the trial. Although there was a trend towards improvement on paired-associate learning performance, which suggested a beneficial effect of centrophenoxine, none of the cognitive tests showed statistically significant improvements with the drug when compared with placebo. However, one subject showed a marked improvement in paired-associate learning test scores which coincided with centrophenoxine administration, and this was mirrored by an increase in the number of words recalled in the first three word-list positions in the word-list recall test. (Recall of the initial words in the list would be expected to provide a more sensitive indicator of improvement than recall of all ten words in the list (Harris & Dowson, 1982).) It may be that more individual case studies with a repeated cross-over design are indicated for this type of investigation, which presents formidable methodological problems.

Centrophenoxine was synthesised in 1959 as the p-chlorphenoxyacetic acid ester of dimethylamino-ethanol. The latter is a precursor of acetyl choline while p-chlorophenoxyacetic acid is related to plant growth hormone. In addition to its effect in reducing the adverse consequences of anoxia, many other effects have been reported such as increased survival time in mice (Hochschild, 1973), an improved learning capacity in animals (Roy *et al*, 1983), increased RNA and protein synthesis in cultural human glial cells (Ludwig-Festl *et al*, 1983), neuronal electrolyte changes (Zs-Nagy *et al*, 1979), increased surface density of synapses in the rat cerebellum (Bertoni-Freddari *et al*, 1982) and increased nucleolar size in the aged rat brain. Several reports have claimed that centrophenoxine increases the activity of the pentose phosphate pathway and also increases the synthesis of phospholipid. It has been suggested that the former is instrumental in rendering the brain less vulnerable to anoxia, while the latter protects membrane proteins against peroxidative damage by free radicals (Bertoni-Freddari *et al*, 1982). Age-related impairment of neuronal structure and function may be partly mediated by an increasing degree of free-radical-induced peroxidation of membrane lipids. This may be the result of the action of several oxidants such as hydrogen peroxide, the superoxide radical and the hydroxyl radical, which arise from the reduction of oxygen. However, antioxidant enzymes such as superoxide dismutase (SOD), catalase, and glutathione peroxidase (GSH-PER) oppose the harmful effects of oxidants. Roy *et al* (1983) investigated the effects of centrophenoxine on the activity of antioxidant enzymes in the rat brain: daily doses of 80 mg/kg and 120 mg/kg for six weeks produced increases in the activity of SOD, GSH-PER and glutathione reductase in each of three brain regions, and the lower dose produced greater changes. It was concluded that centrophenoxine may have a beneficial effect on the function of the aged brain partly due to the activation of certain antioxidant enzymes. These reported effects suggest that long-term prophylactic administration of centrophenoxine might have a role in preventing some of the adverse effects of ageing on neuronal structure and function.

Many studies have claimed that chronic administration of centrophenoxine leads to a reduction in the volume of neuronal lipopigment in many neuronal populations, and that this is accompanied by ultrastructural changes and fragmentation of pigment aggregations. The various reports have involved the examination of histological sections with the light, fluorescence and electron microscopes, and other studies have involved tissue extracts or cell cultures. However, only five light-microscope studies which examined the effects of centrophenoxine on neuronal lipopigment have presented statistical analysis of data: three reported reduced neuronal lipopigment associated with centrophenoxine administration, while two found no significant changes.

Riga & Riga (1974) gave centrophenoxine in a dose of 80 mg/kg by intraperitoneal injection daily for two months to rats aged 24 months. A point-counting method was used to estimate lipopigment volume in 6 μm sections, and the results suggested significant drug-associated reductions in lipopigment volume in five out of six cell populations. Although this was a meticulous study, there were no details of how the cells or fields were selected, the origin of the drug or its medium for solution. Two studies by Nandy (1978*a,b*) reported the effects of daily intraperitoneal injections of 80 mg/kg of centrophenoxine to mice. The duration of treatment varied from 2 to 11 months and the age at sacrifice from 3 to 12 months. Cells of the frontal cortex and hippocampus were examined by a point-counting method, and significant drug-associated effects were reported, although there were no details of the selection or location of the cells, or of many other important aspects of the methodology. It was reported that a significant reduction in neuronal lipopigment occurred after three months of drug treatment.

However, two further studies have produced negative results. Katz & Robison (1983) gave 80 or 120 mg/kg of centrophenoxine intraperitoneally daily for 11 weeks to 25-month-old rats, and lipopigment volume was estimated by a point-counting method involving photographs of neurones of the frontal cortex and of the retinal pigment epithelium. The method was validated by the demonstration of age-related differences in volume of lipopigment, and no drug-related effect was found. Also, Dowson (1985) investigated the effects of daily intraperitoneal injections (80 mg/kg, five days per week) of centrophenoxine in rats over a period of 12 weeks before sacrifice at 13.5 months. No significant effects of centrophenoxine were detected in Purkinje cells or hippocampal neurones using methods which had been validated by the demonstration of differences in lipopigment volume between groups of rats at different ages. This study examined two populations of neurones, the CA3a region of horizontal sections of the hippocampus, and Purkinje cells in Lobule I of the vermis which is easily identified in sagittal sections. It is important to specify which Purkinje cells are examined, as there are significant differences between lobules in the amount of lipopigment in Purkinje cell bodies. Randomly-selected cells were photographed, and the resulting transparencies were then projected onto paper at a constant magnification so that outlines of the areas overlying yellow fluorescent lipopigment could be drawn. The total area enclosed in these outlines, and the number of discrete outlines, were then measured automatically. For relatively small amounts of pigment, this quantitative technique is more accurate than the use of measurements of emitted fluorescence intensity.

At present, no data-containing histological study on the effect of chronic administration of centrophenoxine on mammalian neuronal lipopigment has been reliably confirmed, and further studies need to meet three basic criteria. First, sufficient methodological details must be provided to allow replication; second, particular attention must be paid to the definition and reasonable ease of location of each neuronal population under study; and third, statistically-analysed data must be provided.

Despite the many reported actions of centrophenoxine on the nervous system, there are no clear clinical indications for the use of this drug, and recent studies have not been able to confirm the many original claims that centrophenoxine can reduce neuronal lipopigment. Further research on the effects of this drug, including its effect on neuronal lipopigment, may help to indicate any potential clinical use. If further studies in animal models suggest that centrophenoxine can exert a prophylactic effect on the development of impaired neuronal function and structure due to normal ageing, then a long-term study in man would be indicated. Also, the reports of a dramatic ability of this drug to protect animals from the lethal effects of oxygen deprivation suggest that centrophenoxine may protect the brain, and other organs, from the formation of destructive free radicals during periods of oxygen deprivation. Also, compounds which appear to neutralise free radicals have been identified, and advances in this area could affect the viability of organs for transplantation surgery, and the management of cerebrovascular accidents and coronary thrombosis.

Other effects of centrophenoxine may have potential for therapeutic use: a recent uncontrolled study by Izumi *et al* (1986) claimed that centrophenoxine may be an effective treatment for tardive dyskinesia, and it was suggested that this may be related to an increase in cerebral cholinergic activity. In this study, 7 of 11 patients with tardive dyskinesia or dystonia showed improvements while on daily doses of 600–1200 mg of centrophenoxine, and the movements reappeared 4–8 weeks after medication was discontinued. The maximum effect seemed to occur after about seven weeks of treatment.

Chlorpromazine

Samorajski & Rolsten (1976) administered chlorpromazine to mice over several months and reported that lipopigment granules in neurones of the nucleus reticularis gigantocellularis were markedly less numerous and more dispersed than in control animals, although these observations were not backed up by a validated quantitative methodology. However, drug administration seemed to be associated with a higher mortality. Also, there is a report by Ohtani & Kawashima (1983), which claimed that both chlorpromazine and centrophenoxine reduced the amount of intracellular pigment in cultural rat neurones, so that further histological studies of the effects of long-term chlorpromazine administration are indicated. If these findings are confirmed, it is possible that chronic neuroleptic administration may protect some neurones against certain adverse effects of ageing, although a decrease in neuronal lipopigment could be due to many factors.

Phenytoin

Bernocchi *et al* (1983) claimed that daily administration of phenytoin to rats over eight months was associated with marked increases in the volume of lipopigment in Purkinje cell bodies, and Del Cerro & Snider (1967) reported a similar finding in an ultrastructural study on the effects of phenytoin intoxication. However, this was not confirmed in a recent study (Dowson & Wilton-Cox, 1988), although administration of phenytoin to rats was associated with an increased number of discrete lipopigment particles in Purkinje cells. Also, there are reports of a phenytoin-induced reduction in the number of

Purkinje cells, although this was not shown by Dam (1970) and Dam & Nielson (1970). As neuronal lipopigment accumulation in animal models may be an indication of the toxicity of long-term antiepileptic medication in clinical practice, further studies may prove useful in determining the relative safety of various anticonvulsants and of different dose regimes.

Ethanol

Tavares & Paula-Barbosa (1983) administered a 20% aqueous ethanol solution to rats for periods of up to 18 months and claimed that Purkinje cell bodies contained considerably more lipopigment than in controls, although this was not confirmed by Dowson & Wilton-Cox (1988). Also Borges *et al* (1986) reported that administration of a similar ethanol solution was associated with an increased lipopigment volume in hippocampal neurones after three months. Further studies in animal models may lead to an understanding of mechanisms responsible for the more subtle clinical features of alcohol abuse.

Future studies

Future studies of neuronal lipopigment may contribute to the study of ageing, ageing-related vulnerability to various diseases, functional activity of neurones, pathogenic mechanisms, the effects of psychotropic drugs, and the possible clinical applications of drugs which modify neuronal lipopigment.

Of the various drugs which have been used clinically, and which have been examined in respect of their effect on lipopigment, centrophenoxine is of particular interest, as many reports have claimed that long-term use of this compound is associated with a relatively small volume of neuronal lipopigment. However, conflicting results indicate the need for further investigations. If drug regimes can be identified which can consistently reduce the accumulation of neuronal lipopigment in animal models, these would be candidates for clinical trials in an increasingly elderly population, both in the healthy elderly and in early dementia.

The prophylactic effect of lipopigment-reducing regimes on normal elderly individuals could be examined in respect of the cognitive impairments which have been described in many elderly individuals without disease, although it should be noted that the effect of antioxidant dietary supplements may not significantly affect the maximum lifespan of a species (Pryor, 1982). However, lipopigment-reducing drugs might minimise various adverse effects of the ageing process, leading to an increase (perhaps of several years) in the mean lifespan, together with a reduced susceptibility to a variety of diseases and degenerative changes. Such effects may occur even if accumulation of lipopigment is not, in itself, harmful.

Although there is no evidence that any drug can modify the survival time of a patient with dementia, Halliwell & Gutteridge (1984) have pointed out that diseased tissue may undergo increased damage in a process which involves cytotoxic end-products of lipid peroxidation and increased lipopigment formation. Antioxidants, free-radical neutralisers, or drugs which reduce lipopigment accumulation, might have a beneficial effect in a process of neuronal degeneration by preventing any such secondary damage, although the primary pathogenic mechanisms of the disease would not be halted. Therefore, drugs which lead to a reduced accumulation of neuronal lipopigment might exert a beneficial effect on neuronal function in various degenerative diseases, without affecting the survival time. The effects of such drugs could be investigated in the relatively early stages of dementia, when the maximum number of neurones would be present and the degree of functional impairment would be relatively slight.

However, this is likely to produce, at best, only modest clinical benefits, and investigating the effects of lipopigment-reducing drugs in relation to normal ageing, ageing-related susceptibility to various diseases and anoxic conditions would seem to hold out more promise of real clinical benefit.

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References

BADURSKA, B., FIDZIANSKA, A. & JEDRZEJOWSKA, H. (1981) A dominant form of neuronal ceroid-lipofuscinosis. *Journal of Neurology*, **226**, 205–212.

BASSON, A. B. K., TERBLANCHE, S. E. & OELOFSEN, W. (1982) A comparative study on the effects of ageing and training on the levels of lipofuscin in various tissues of the rat. *Comparative Biochemical Physiology*, **71**, 369–374.

BERNOCCHI, G., BOTTIROLI, G., CAVANNA, O., *et al* (1983) Fluorescence histochemical patterns of Purkinje cell layer in rat cerebellum after long-term phenytoin administration. *Basic and Applied Histochemistry*, **27**, 45–53.

BERTONI-FREDDARI, C., GIULI, C. & PIERI, C. (1982) The effect of acute and chronic centrophenoxine treatment on the synaptic plasticity of old rats. *Archives of Gerontology and Geriatrics*, **1**, 363–373.

BOEHME, D. H., COTTELL, J. C., LEONBERG, S. C., *et al* (1971) A dominant form of neuronal ceroid-lipofuscinosis. *Brain*, **94**, 745–760.

Borges, M. M., Paula-Barbosa, M. M. & Volk, B. (1986) Chronic alcohol consumption induces lipofuscin deposition in the rat hippocampus. *Neurobiology of Aging*, **7**, 347–355.

Braak, H. & Goebel, H. N. (1979) Pigmentoarchitectonic pathology of the isocortex in juvenile neuronal ceroid-lipofuscinosis: axonal enlargements in layer IIIab and cell loss in layer V. *Acta Neuropathologica*, **46**, 79–83.

Brizzee, K. R. (1975) Ageing changes in relation to diseases of the nervous system. In *Neurobiology of Ageing* (eds J. M. Ordy & K. R. Brizzee). New York: Plenum Press.

——, Kaack, B. & Klara, P. (1975) Lipofuscin: intra and extraneuronal accumulation and regional distribution. In *Neurobiology of Ageing* (eds J. M. Ordy & K. R. Brizzee). New York: Plenum Press.

—— & Knox, C. (1980) The ageing process in the neurone. *Advances in Experimental Medicine and Biology*, **129**, 1–98.

Chou, S. M. & Thompson, H. G. (1970) Electron microscopy of storage cytosomes in Kufs' disease. *Archives of Neurology (Chicago)*, **23**, 489–501.

Constantinides, P., Harkey, M. & McLaury, D. (1986) Prevention of lipofuscin development in neurones by anti-oxidants. *Virchows Archives*, **409**, 583–593.

Dam, M. (1970) Number of Purkinje's cells after diphenylhydantoin intoxication in pigs. *Archives of Neurology*, **22**, 64–67.

—— & Nielson, M. (1970) Purkinje's cells density after diphenylhydantoin intoxication in rats. *Archives of Neurology*, **23**, 555–557.

Del Cerro, M. P. & Snider, R. S. (1967) Studies on dilantin intoxication–1. Ultrastructural analogies with lipoidoses. *Neurology*, **17**, 452–466.

Dom, R., Brucher, J. M., Ceuterick, C., *et al* (1979) Adult ceroid-lipofuscinosis (Kufs' disease) in two brothers. *Acta Neuropathologica (Berlin)*, **45**, 67–72.

Dowson, J. H. (1982*a*) The evaluation of autofluorescence emission spectra derived from neuronal lipopigment. *Journal of Microscopy*, **128**, 261–270.

—— (1982*b*) Neuronal lipofuscin accumulation in ageing and Alzheimer dementia: A pathogenic mechanism? *British Journal of Psychiatry*, **140**, 142–148.

—— (1983) Autofluorescence emission spectra of neuronal lipopigment in a case of adult-onset ceroidosis (Kufs' disease). *Acta Neuropathologica*, **59**, 241–245.

—— (1985) Quantitative studies on the effects of ageing, meclofenoxate, and dihydroergotoxine on intraneuronal lipopigment accumulation in the rat. *Experimental Gerontology*, **20**, 333–340.

—— & Harris, S. J. (1981) Quantitative studies of the autofluorescence derived from neuronal lipofuscin. *Journal of Microscopy*, **123**, 249–258.

——, Armstrong, D., Koppang, N., *et al* (1982) Autofluorescence emission spectra of neuronal lipopigment in animal and human ceroidoses (ceroid-lipofuscinoses). *Acta Neuropathologica*, **58**, 152–156.

—— & Wilton-Cox, H. (1988) The effect of drugs on neuronal lipopigment. In *Lipofuscin – 1987: State of the Art* (ed. I. Zs-Nagy), pp 271–288. Amsterdam: Elsevier Science Publishers.

Earnest, M. P., Heaton, R. K., Wilkinson, W. S., *et al* (1979) Cortical atrophy, ventricular enlargement and intellectual impairment in the aged. *Neurology*, **29**, 1138–1143.

Freund, G. (1979) The effects of chronic alcohol and vitamin E consumption on ageing pigments and learning performance in mice. *Life Science*, **24**, 145–152.

Gedye, J. L., Exton-Smith, A. N. & Wedgewood, J. (1972) A method for measuring mental performance in the elderly and its use in a pilot clinical trial of meclofenoxate in organic dementia. *Age and Ageing*, **1**, 74–80.

Glees, P. & Spoerri, P. E. (1975) Centrophenoxin-induced dissolution and removal of lipofuscin: an electron microscopic study. *Arzneimittel-Forschung*, **25**, 3–9.

Glick, R. & Bondareff, W. (1979) Loss of synapses in the cerebellar cortex of the senescent rat. *Journal of Gerontology*, **24**, 818–822.

Goebel, H. H., Pilz, H. & Gullotta, F. (1976) The protracted form of juvenile neuronal ceroid-lipofuscinosis. *Acta Neuropathologica*, **36**, 393–396.

Halliwell, B. & Gutteridge, J. M. C. (1984) Lipid peroxidation, oxygen radicals, cell damage, and antioxidant therapy. *Lancet*, *i*, 1396–1397.

Harris, S. J. & Dowson, J. H. (1982) Recall of a 10-word list in the assessment of dementia in the elderly. *British Journal of Psychiatry*, **141**, 524–527.

—— & —— (1986) The effects of meclofenoxate on cognitive performance in elderly individuals with memory impairment: a placebo-controlled study. *International Journal of Geriatric Psychiatry*, **1**, 93–98.

Hittner, H. M. & Zeller, R. S. (1975) Ceroid-lipofuscinosis (Batten disease). *Archives of Opthalmology*, **93**, 178–183.

Hochschild, R. (1973) Effect of dimethylaminoethyl p-chlorophenoxyacetate on the life span of male Swiss Webster albino mice. *Experimental Gerontology*, **8**, 177–183.

Huber, F., Koberle, S., Prestele, H., *et al* (1986) Effects of long-term ergoloid mesylates (Hydergine) administration in healthy pensioners: 5 year results. *Current Medical Research and Opinion*, **10**, 256–279.

Izumi, K., Tominaga, H., Koja, T., *et al* (1986) Meclofenoxate therapy in tardive dyskinesia: a preliminary report. *Biological Psychiatry*, **21**, 151–160.

Johnson, E. M., Palmatier, M. A., Rydel, R. E., *et al* (1986) Species and structural specificity of the lipopigment accumulation and neuronal destruction induced by N (2-guanidinoethyl)-4-methyl-1,2,5,6-tetrahydropyridine. (Guanacline). *Brain Research*, **383**, 100–109.

Karnaukhov, U. N. (1972) On the nature and function of yellow aging pigment lipofuscin. *Experimental Cell Research*, **80**, 479.

Katz, M. L. & Robison, W. G. (1983) Lipofuscin response to the 'aging-reversal' drug centrophenoxine in rat retinal pigment epithelium and frontal cortex. *Journal of Gerontology*, **38**, 525–531.

——, ——, Herrmann, R. K., *et al* (1984) Lipofuscin accumulation resulting from senescence and vitamin E deficiency: spectral properties and tissue distribution. *Mechanisms of Ageing and Development*, **25**, 149–159.

Kent, S. (1976) Solving the riddle of lipofuscin origin may uncover clues to the ageing process. *Geriatrics*, **May**, 128–137.

Kerenyi, T., Haranghy, L. & Huttner, I. (1968) Investigations on experimentally produced age-pigment in the nervous system. *Experimental Gerontology*, **3**, 155–158.

Kornfeld, M. (1972) Generalized lipofuscinosis (generalized Kufs' disease). *Journal of Neuropathology and Experimental Neurology*, **3**, 608–682.

Lowden, J. A., Callahan, J. W., Gravel, R. A., *et al* (1981) Type 2 GM$_1$ gangliosidosis with long survival and neuronal ceroid lipofuscinosis. *Neurology (NY)*, **31**, 719–724.

Ludwig-Festl, M., Grater, B. & Bayreuther, K. (1983) Meclofenoxate-induced increase in cell metabolic activities in normal diploid human glia cells in a stationary cell culture system. *Arzneimittel-Forschung*, **33**, 495–501.

Malamud, N. (1972) Neuropathology of organic brain syndromes associated with ageing. *Advances in Behavioural Biology*, **3**, 63–88.

Mann, D. M. A. & Yates, P. O. (1974) Lipoprotein pigments – their relationship to ageing in the human nervous system. *Brain*, **97**, 481–488.

——, —— & Barton, C. M. (1977) Cytophotometric mapping of neuronal changes in senile dementia. *Journal of Neurology, Neurosurgery and Psychiatry*, **40**, 299–302.

—— & Sinclair, K. G. A. (1978) The quantitative assessment of lipofuscin pigment, cytoplasmic RNA and nucleolar volume in senile dementia. *Neuropathology and Applied Neurobiology*, **4**, 129–135.

——, Yates, P. O. & Stamp, J. E. (1978) The relationship between lipofuscin pigment and ageing in the human nervous system. *Journal of Neurological Sciences*, **37**, 83–93.

Marcer, D. & Hopkins, S. M. (1977) The differential effects of meclofenoxate on memory loss in the elderly. *Age and Ageing*, **6**, 123–131.

McBrien, D. C. H. & Slater, T. F. (eds) (1982) *Free Radicals, Lipid Peroxidation and Cancer*. London: Academic Press.

McDonald, C. (1969) Clinical heterogeneity in senile dementia. *British Journal of Psychiatry*, **115**, 267–271.

Miyazaki, H., Nambu, K. & Hashimoto, M. (1976) Antianoxic effect of meclofenoxate related to its disposition. *Chemical and Pharmacological Bulletin*, **24**, 822–825.

Monagle, R. D. & Brody, H. (1974) The effects of age upon the main nucleus of the inferior olive in the human. *Journal of Comparative Neurology*, **155**, 61–66.

Nandy, K. (1978*a*) Lipofuscinogenesis in mice early treated with centrophenoxine. *Mechanisms in Ageing and Development*, **8**, 131–138.

—— (1978*b*) Centrophenoxine: effects on ageing mammalian brain. *Journal of the American Geriatrics Society*, **26**, 74–81.

—— & Schneider, F. H. (1978) Effects of hydergine on aging neuroblastoma cells in culture. *Pharmacology*, **16**, 88–92.

Ohtani, R. & Kawashima, S. (1983) Reduction of lipofuscin by centrophenoxine and chlorpromazine in the neurones of rat cerebral hemisphere in primary culture. *Experimental Gerontology*, **18**, 105–112.

Oldfors, A. & Sourander, P. (1981) Storage of lipofuscin in neurones in mucopolysaccheridoses. *Acta Neuropathologica*, **54**, 287–292.

Oliver, J. E. & Restell, M. (1967) Serial testing in assessing the effect of meclofenoxate on patients with memory defects. *British Journal of Psychiatry*, **113**, 219–222.

Pallis, C. A., Duckett, S. & Pearce, A. G. E. (1967) Diffuse lipofuscinosis of the central nervous system. *Neurology (NY)*, **17**, 381–395.

Paoiorek, P. M. & Wyllie, M. G. (1980) The effects of drugs on cerebral cortex ATP levels in normal and hypoxic rats. *British Journal of Pharmacology*, **70**, 92–93.

Papafrangos, E. S. & Lyman, C. P. (1982) Lipofuscin accumulation and hibernation in the Turkish Hamster, Mesocricetus trandti. *Journal of Gerontology*, **37**, 417–421.

Pryor, W. A. (1982) Free radical biology: xenobiotics, cancer and aging. *Annals of the New York Academy of Sciences*, **393**, 1–22.

Rapin, I., Suzuki, K. & Valsarnis, M. P. (1976) Adult (chronic) GM_2 gangliosidosis. *Archives of Neurology*, **33**, 120–130.

Riga, S. & Riga, D. (1974) Effects of centrophenoxine on the lipofuscin pigments in the nervous system of old rats. *Brain Research*, **72**, 265–275.

Roy, D., Pathak, D. N. & Singh, R. (1983) Effects of centrophenoxine on the antioxidative enzymes in various regions of the aging rat brain. *Experimental Gerontology*, **18**, 185–197.

Rudra, D. N., Dickerson, J. W. T. & Walker, R. (1975) The effect of some antioxidants on lipofuscin accumulation in rat brain. *Proceedings of the Nutrition Society*, **34**, 122.

Samorajski, T. & Rolsten, C. (1976) Chlorpromazine and ageing in the brain. *Experimental Gerontology*, **11**, 141–147.

Sandoz, P. & Meier-Ruge, W. (1977) Age-related loss of nerve cells from the human inferior olive, and unchanged volume of its grey matter. *IRCS (International Research Communications System) Journal of Medical Sciences*, **5**, 376.

Scholtz, C. L. & Brown, A. (1978) Lipofuscin and transynaptic degeneration. *Virchows Archives*, **281**, 35–40.

Suzuki, Y., Furukawa, T., Hoogeuben, A., *et al* (1979) Adult type GM_1 gangliosidosis: a complementation study on somatic hybrids. *Brain Development*, **1**, 83–86.

Tavares, M. A. & Paula-Barbosa, M. M. (1983) Lipofuscin granules in Purkinje cells after long-term alcohol consumption. *Alcoholism: Clinical and Experimental Research*, **7**, 302–306.

Totaro, E. A., Pisanti, F. A., Continillo, A., *et al* (1985) Morphological evaluation of the lipofuscinolytic effect of acetylhomocysteine thiolactone. *Archives of Gerontology and Geriatrics*, **4**, 67–72.

Wechsler, D. (1958) *The Measurement and Appraisal of Adult Intelligence*, London: Balliere, Tindall and Cox.

West, C. D. (1979) A quantitative study of lipofuscin accumulation with age in normals and individuals with Down's syndrome, phenylketonuria, progeria and transneuronal atrophy. *Journal of Comparative Neurology*, **186**, 109–116.

Yamada, M. (1978) On the distribution of senile changes in the spinal cord. *Folia Psychiatrica et Neurologica Japonica*, **32**, 249–251.

Yesavage, J. A., Tinklenberg, J. R., Hollister, L. E., *et al* (1979) Vasodilators in senile dementias. *Archives of General Psychiatry*, **36**, 220–232.

Zeman, W. (1976) The neuronal ceroid-lipofuscinoses. In *Progress in Neuropathology, Vol. III* (ed. H. H. Zimmerman). New York, San Francisco, London: Grune and Stratton.

—— & Hoffman, J. (1962) Juvenile and late forms of amaurotic idiocy in one family. *Journal of Neurology, Neurosurgery and Psychiatry*, **25**, 352–362.

Zs-Nagy, I., Pieri, C. & Del Moro, M. (1979) Effects of centrophenoxine on the monovalent electrolyte contents of the large brain cortical cells of old rats. *Gerontology*, **25**, 94–102.

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The Evaluation of Mental Health Care Systems

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While the demand for deinstitutionalisation, strongly supported by the economic aspect of the issue, has resulted in a steep decline in the number of psychiatric beds in many Western countries, the evaluation of extramural psychiatric care has several difficulties, including that of proving effectiveness without experimental control of confounding influences. For a cohort of schizophrenic patients we investigated the impact of out-patient psychiatric treatment on length of stay in hospital and length of stay in the community. Out-patient care had a significant influence on readmission, but no effect on the length of in-patient treatment. While the average cost of community care was less than half that of traditional hospital care, in 6% of the patients this threshold value of continued in-patient care was exceeded. There also seems to be a non-monetary threshold, above which community care is no longer appropriate.

Apart for a few isolated hospitals such as Casa de Orates in Valencia, founded in 1409, institutional mental health care began in the 18th and 19th centuries. The aim was to provide better accommodation and care for the incurably mentally ill than the medieval prisons, workhouses, and impoverished relatives were able to offer. Subsequently long-stay patients and bed occupancy in mental hospitals increased continuously in industrialised societies. Although pre-eminent psychiatrists such as Griesinger (1845) in Germany warned of its disastrous consequences, the idealistic model of a remote mental hospital (to rescue the mentally ill from the allegedly pathogenic environment) became the archetype of a large number of mental hospitals in Europe.

The expansion of custodial mental health care and the accumulation of psychiatric beds peaked in the middle of this century. In 1955 the number of occupied beds in psychiatric hospitals stood at about 350 per 100 000 population in Great Britain and at about 450 per 100 000 in the USA. Thereafter the rates declined steeply to about 155 per 100 000 in England and Wales on a census day in 1981 (Department of Health and Social Security, 1980; British Psychiatric Register Group, 1984) and 96 per 100 000 in the USA in 1983 (National Institute of Mental Health, 1987).

The three main reasons for the new trend in the system of mental health care – 'deinstitutionalisation' – are: (a) the scandalous neglect of mental hospitals; (b) the transition of psychiatry to a primarily therapeutic discipline; and (c) the *Zeitgeist* stressing civil rights and demanding an optimum of freedom and quality of life for the chronically ill and disabled. The demand for deinstitutionalisation has been intensified by the economic aspect of the issue. In the USA over $30 billion was spent on psychiatric services in 1980 (Talbott, 1985). Almost 25% of all the days spent in hospital were accounted for by mental patients, and 70% of the funds allocated to mental health care were spent on in-patient care (Mosher, 1983).

The deinstitutionalisation movement, however, failed to see the risks of discharging chronic patients with social disabilities to the community, where their families could not provide them with adequate support or where there was insufficient alternative residential care.

Evaluating the success of deinstitutionalisation is controversial (Gralnick, 1985; Okin, 1985), as is the extent to which extramural care should be expanded and to what extent in-patient care is still needed. In this far-reaching transition to new patterns of mental health care, monitoring outcome and evaluating of the effectiveness of alternative strategies are of crucial importance.

Monitoring changes in a mental health care system

Although aggregate data do not distinguish multiple utilisations of services by individual patients, they can be used for monitoring the utilisation of mental health care systems (National Institute of Mental Health, 1986, 1987) and for global cost analyses. The almost tenfold increase in episodes of out-patient care that took place in the USA between 1955 and 1975, as well as a slight fall in the overall utilisation of mental health services since 1975, reflect the enormous changes in the national system of mental health care (Redick *et al*, 1985).

Nationwide out-patient data on specialist services are available in only a few countries, and hardly any nationwide data exist on the utilisation of primary health care, a fact that is in contrast with the importance of this sector for the mentally ill. A cross-sectional study conducted in the state of Bayern, West Germany (population nine million), showed that in 1983 almost half of the members of the largest health insurance scheme in West Germany who were admitted to in-patient care for mental disorders were cared for in non-psychiatric units, primarily those specialising in internal medicine (Hospital Management, 1985). The quality of care provided by non-psychiatric health services is not usually considered when evaluating mental health care systems.

The contributions of case registers to service research (Wing & Fryers, 1976; British Psychiatric Register Group, 1984; ten Horn *et al*, 1986) are most valuable at the local level, where their catchment areas are identical with those of community mental health services. In a comparative description of data from eight British case registers covering 1976–81 (British Psychiatric Register Group, 1984), the admission rates of people over 64 years increased by 6% to 41% in the catchment areas of six out of eight registers. With one exception the proportion of short-stay patients (one-year maximum) rose in all register areas, whereas 'very-long-stay' patients (over five years) decreased almost everywhere. Four out of six registers that recorded the contacts with psychiatric out-patient clinics for the whole period of observation reported an increase in utilisation rates of between 7.6% and 21.3%.

Evaluating the effectiveness of mental health care

A descriptive evaluation of mental health care should detail service utilisation and service provision by certain standards or through comparative data. Output evaluation (Suchman, 1967) aims at proving the effectiveness of mental health services or programmes, but whereas the efficacy of antipsychotic medication in the treatment of schizophrenic patients seems well established (Leff & Wing, 1971; Hirsch *et al*, 1973: Hogarty & Goldberg, 1973), the mode of action of facilities or subsystems of care is far less certain.

Most studies on the effectiveness of extramural health care for chronic mental patients are based on "synthesized community support systems" (Bachrach, 1982) – "interventions planned to test hypotheses, to elaborate on the conditions under which selected variables have specific outcomes", as opposed to "organic community support systems"–the "answers to a community's perceived needs," reflecting the problems and conditions of the community in which they are found. While the former often serve their purpose effectively (e.g. Davis *et al*, 1972; Stein *et al*, 1975), they may not substitute the analysis of 'organic' care systems. The latter, however, often fail to describe the actual care provided in a reproducible way or to analyse it with regard to its main components; neither have the patient samples been defined precisely enough with regard to diagnosis, degree of severity, or chronicity in most of the studies. These shortcomings explain why studies evaluating the effectiveness of 'organic' extramural psychiatric care are often contradictory with respect to their effects on outcome (an der Heiden *et al*, 1989).

In order to arrive at realistic and more generalisable results, the following criteria must be heeded: (a) interventions subject to evaluation must be described precisely; (b) the patient population studied should be homogeneous with respect to the relevance of the therapeutic interventions and the outcome variables; and (c) there should be a clear definition of the therapeutic objectives. As one objective is to substitute in-patient treatment by extramural care, possible outcome criteria may be number of readmissions and days spent in hospitals, or length of stay in the community. In order to assure that a lack of readmissions means more efficient, successful treatment, one has also to control for illness-related measures as symptoms, social competence and independence, and burden on the patient's family or the community and life satisfaction.

A classic way of controlling variables confounding the relationship between intervention and outcome is a random assignment of patients to certain treatment conditions (a model programme of extramural mental health care) and control conditions (the traditional care provided in the area where the study is conducted, or continued hospital care). However, the classic experimental criteria, such as manipulation and variation of independent variables, control of intervening variables, and replicability, frequently cannot be fulfilled in evaluative studies. One of the main reasons is ethical objections to a strictly random assignment of patients.

In a critical evaluation of 18 studies, Braun *et al* (1981) found that the internal and external validity of the results in the majority of the studies reviewed had to be questioned because of shortcomings in study design or assignment of patients. The authors concluded that the superiority of alternative programmes to the traditional forms of mental health care could not be proven in any of the studies referred to. The model programmes, on which most of the studies were based, frequently failed to specify whether the reported decreases in readmissions resulted from an improvement in the patient's status, or from an increased tolerance in the patient's environment created by the model programme. The fact that in many experimental studies the positive effects disappeared after a short time (Langsley *et al*, 1971; Davis *et al*, 1972; Mosher & Menn, 1978; Test & Stein, 1978) could also be explained by the 'Hawthorne effect', that is, the effect of motivation by a new approach which cannot be preserved in the long run (Mechanic, 1978; Bachrach, 1980).

Because of the impracticability of a random assignment, one has to look for alternative strategies to control for intervening variables. To rule out alternative interpretations of empirical data in a naturalistic design, intervening variables can be controlled only on the basis of a theoretical model, taking into account the supposed interactions. One precondition is that most relevant variables are known.

We investigated the effect of one particular component of the extramural care provided for schizophrenic patients – out-patient psychiatric care – on the time spent outside hospital and the length of stay after readmission.

Experimental

The cohort included all patients from the Mannheim population who were successively admitted to hospital during one year (1977–78) with the diagnosis of schizophrenia. The cohort of 148 schizophrenics was interviewed at intervals of six months, during a study period of 18 months, to obtain information on symptoms and use of extramural services.

In line with the model of analysis (Fig. 1), symptoms when entering the study, length of in-patient care received up to that time, and living conditions (living in a psychiatric home, with relatives, or alone) were used as intervening variables. The effects of these intervening variables on the observed values of the independent and dependent variables were computed by regression analysis and partialled out.

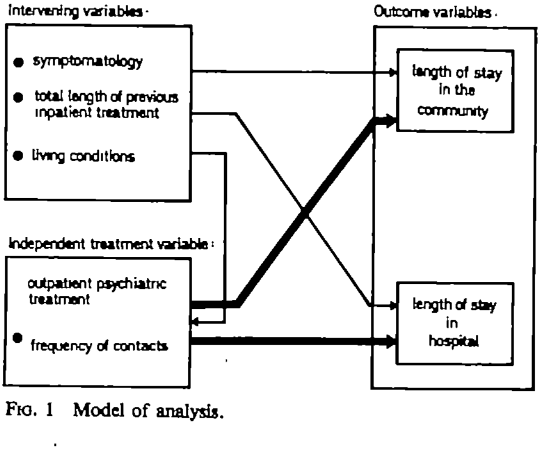
Intervening variables ·
symptomatology
total length of previous inpatient treatment
living conditions
Independent treatment variable :
outpatient psychiatric treatment
frequency of contacts
Outcome variables ·
length of stay in the community
length of stay in hospital

Fig. 1 Model of analysis.

Figure 2 shows the results of a survival analysis (Kalbfleisch & Prentice, 1980) for the interval between discharge from hospital to readmission, or to the end of the study period, for different frequencies of out-patient psychiatric contacts. As values for the independent variable, we chose the first, fifth and ninth decile of the distribution. The graph in Fig. 2 shows a highly significant ($P < 0.01$) influence of out-patient psychiatric treatment on the probability of readmission. For example, the difference between the median survival time of the first decile (low frequency of out-patient contacts) and the fifth decile (medium frequency) is over 160 days.

An examination of the effect of out-patient care on the dependent variable 'length of in-patient treatment' (Fig. 3) revealed no difference between the three groups. This means that out-patient mental health care does not exert any influence on the length of in-patient treatment at

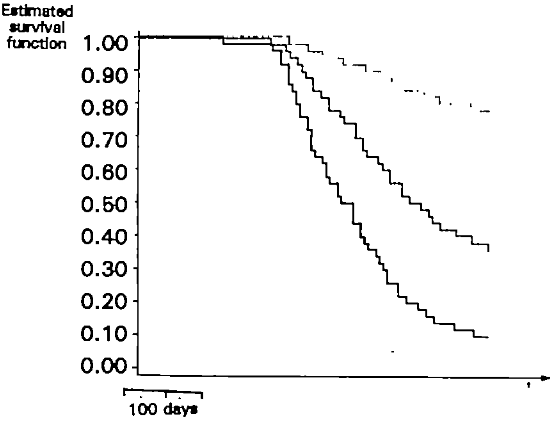

Fig. 2 Survival analysis: the effect of 'frequency of out-patient psychiatric contacts' (— low frequency, - - - medium, ... high) on length of stay in the community.

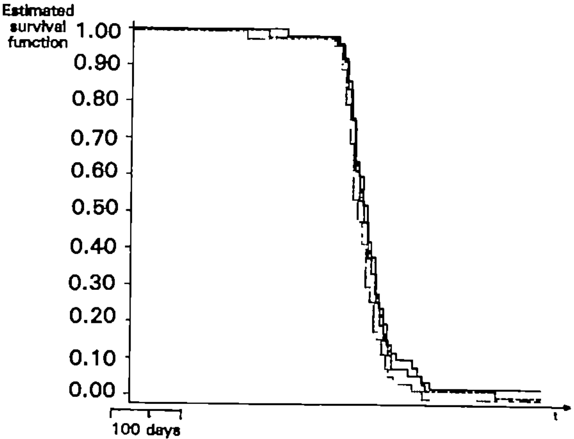

Fig. 3 Survival analysis: the impact of 'frequency of out-patient psychiatric contacts' (— low frequency, - - - medium, ... high) on length of stay in hospital.

readmission: length of hospital stay is probably influenced more by the course of symptoms at relapse and by hospital variables.

We then studied the effect of extramural medical care on total need for in-patient treatment and on symptoms. The study period of 18 months was divided into 12 and 6 months. Using a similar model as described above to partial out intervening influences (see Fig. 1), a significant negative correlation between the frequency of out-patient contacts in the first 12 months and total length of in-patient treatment in the subsequent six months emerged ($r = -0.32$, $P < 0.001$). In the same way, we also studied the effects of out-patient care on the disease variables. Again, we found significant negative correlations with symptoms and disease-related behaviour, measured by BSO (behaviour, speech, and other disorders) and DAH (delusions and hallucinations), the syndrome indices of the Present State Examination (PSE; Wing *et al*, 1974).

In order to assess the differential effects of the patient's setting in the community on the impact of out-patient psychiatric treatment, we subdivided the cohort into three groups according to living conditions (Table I). For patients living in sheltered accommodation, we found that more psychiatric out-patient treatment resulted in a decrease both in in-patient treatment and in the two syndrome scores. Looking only at the disease-related measures, for patients living with their families, the correlation was much smaller, whereas for patients living alone no significant effect could be found. We assume that the indirect effect of living conditions on the effectiveness of out-patient care had something to do with a better compliance with prescriptions in a better-supervised setting, as all psychiatric homes in Mannheim are visited at least once a month by a psychiatrist or a social worker.

TABLE I

Effect of out-patient psychiatric treatment on length of stay in hospital and symptoms[1]

Months 1–12	*Months 13–18*		
	In-patient treatment[2]	*PSE subscore* *DAH*[3]	*BSO*[3]
Living alone ($n = 32$)[4]	−0.31*	0.00	−0.01
Living in family ($n = 68$)[4]	−0.29**	−0.14*	−0.08
Living in sheltered accommodation ($n = 25$)[4]	−0.40**	−0.35*	−0.27*

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1. Pearson correlations after removing the effects of 'symptoms' and 'chronicity of illness' by regression analysis; sample broken down by living conditions.
2. No. of intervals.
3. Total score.
4. Only patients with complete information.

*$P < 0.05$, **$P < 0.01$.

Cost aspects as indicators of the functioning of the extramural mental health care system

The study of the costs of mental health care, especially the comparison of extramural psychiatric care with the traditional hospital care of chronic mental patients, is of importance for administrative decisions and for evaluating certain forms of care. The quantified utilisation data of our cohort of 148 patients was the basis for a case-related calculation of the costs of treatment. They consist of the direct costs of full and partial hospital care, out-patient medical care, daily rates for psychiatric homes, and rehabilitation units etc. based on 1980 prices. When we compared the mean costs of comprehensive community care per case in our cohort (including the costs of hospital readmissions) with those of continued hospital care of the same length, community care cost less than half as much as traditional care (Fig. 4).

However, when the costs of complementary care for individual cases were looked at, distributed over the total number of cases, a steeply rising trend emerged, which finally exceeded the threshold value represented by the costs of continued in-patient care. In eight cases (6% of the cohort) the cost of complementary care was higher than that of traditional hospital care.

The results of our comparison of average costs are valid only under the condition that 40% of all schizophrenic long-stay (over one year) patients are admitted (Häfner & an der Heiden, 1983). Of all schizophrenic patients in Mannheim needing long-term care of more than one year in 1980, about three-quarters were admitted to sheltered accommodation, and only a quarter to a mental hospital. Community mental health care, as compared with continued hospital care, becomes considerably cheaper if severely ill and disabled patients needing particularly intensive care are not discharged from hospital. The

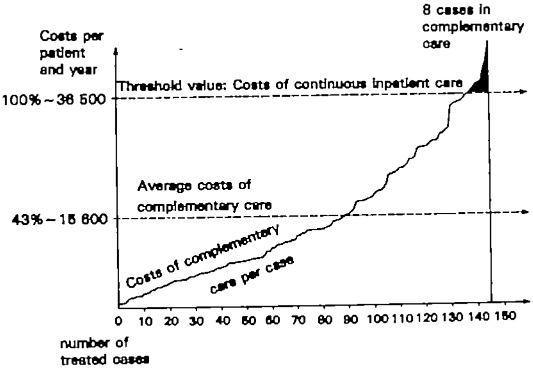

FIG. 4 Direct costs of community care (based on 1980 prices).

steep increase in cost per case indicates that with increasing needs for care, which are probably accounted for by severe mental disorder, the monetary costs (and probably also the non-monetary costs, i.e. the burden to the patients themselves, their families, and the community services) exceed the costs of hospital care. Thus there is not only a monetary, but also a non-monetary threshold value, above which community care seems to be no longer appropriate. Beyond this threshold it is not only cheaper, but probably also more humane to place chronically ill patients requiring long-term in-patient care in mental hospitals providing 24-hour medical and nursing care, good accommodation, occupation, and leisure-time activities, as well as rehabilitation units.

The distribution of costs per case shows that in patient groups with supposedly similar needs, the intensity of institutionalised care needed varies considerably (Mechanic, 1987). In the transition from a hospital-centred to a community-centred mental health care system, milder cases are probably discharged first, but with a growing proportion of chronic patients discharged from hospital into the community, the number of more severely disordered out-patients increases, and as service use in out-patient psychiatric care is directly related to the measure of need (Goldman & Taube, 1988), the cost per case increases. In-patient care will also change. The proportion of long-stay patients needing less intensive care and nursing will decline. The small proportion of new long-stay in-patients will require more intensive care. In fact, all patients in need of in-patient care, in spite of the availability of a dense network of complementary services, will require more intensive care, as many of them will not be readmitted until their episode of illness is sufficiently severe (Hoult, 1986). This means that both the psychiatric unit serving acutely ill mental patients and the mental hospital ward serving chronic patients have to provide more intensive care and a better standard of service than did the traditional mental health care system. The results of a comparative evaluation of the effectiveness and costs of the two components of the system depend on how far this process has advanced, and how many severely ill discharged chronic patients need intensive community care. This has been neglected in several studies.

Conclusion

Such far-reaching, rapid changes as the system of mental health care is currently undergoing are associated with high risks. They should not be allowed to result from an uncontrolled manipulation on purely political or economic grounds. A descriptive monitoring of mental health care by means of nationwide health statistics, and the evaluation of the effectiveness of whole packages or individual components of new forms of care and their costs, is presently needed in psychiatry more urgently than in any other sector of public health. It should be remembered that changes in one sector, such as the expansion of extramural care, will produce changes in other sectors, such as hospital care.

References

an der Heiden, W., Häfner, H. & Krumm, B. (1989) *Die Wirksamkeit Ambulanter Psychiatrischer Versorgung. Ein Modell zur Evaluation Extramuraler Dienste*. Berlin/Heidelberg/New York: Springer.

Bachrach, L. (1980) Overview: model programs for chronic patients. *American Journal of Psychiatry*, **137**, 1023–1031.

—— (1982) Assessment of outcome in community support system: results, problems and limitations. *Schizophrenic Bulletin*, **8**, 39–61.

Braun, P., Kochansky, G., Shapiro, R., *et al* (1981) Overview: deinstitutionalization of psychiatric patients, a critical review of outcome studies. *American Journal of Psychiatry*, **138**, 736–749.

British Psychiatric Register Group (1984) *Psychiatric Care in 8 Register Areas: Statistics from 8 psychiatric case registers in Great Britain, 1976–1981*. Southampton: British Psychiatric Register Group, c/o Knowle Hospital.

Davis, A., Dinitz, S. & Pasamanick, B. (1972) The prevention of hospitalization in schizophrenia: five years after an experimental program. *American Journal of Orthopsychiatry*, **42**, 375–388.

Department Of Health And Social Security (1980) *In-patient Statistics from the Mental Health Inquiry for England 1977*. Statistical Report Series no. 23. London: HMSO.

Goldman, H. H. & Taube, C. A. (1988) High users of outpatient mental health services, II: Implications for practice and policy. *American Journal of Psychiatry*, **145**, 24–28.

Gralnick, A. (1985) Build a better state hospital: deinstitutionalization has failed. *Hospital and Community Psychiatry*, **36**, 738–741.

Griesinger, W. (1845) *Die Pathologie und Therapie der Psychischen Krankheiten*. Stuttgart: Krabbe.

Hafner, H. & an der Heiden, W. (1983) The impact of a changing system of care on patterns of utilization by schizophrenics. *Social Psychiatry*, **18**, 153–160.

Hirsch, S. R., Gaind, R., Rohde, P. D., *et al* (1973) Outpatient maintenance of chronic schizophrenic patients with long-acting fluphenazine: double-blind placebo trial. *British Medical Journal*, *i*, 633–637.

Hogarty, G. E. & Goldberg, S. C. (1973) Drug and sociotherapy in the aftercare of schizophrenic patients. *Archives of General Psychiatry*, **28**, 4–64.

Hospital Management (1985) *Patientenstrukturanalyse Psychiatrie Bayern*; scientific evaluation by Prof. D. Böcker (Bayreuth) (in press).

Hoult, J. (1986) Community care for the acutely mentally ill. *British Journal of Psychiatry*, **149**, 137–144.

Kalbfleisch, J. D. & Prentice, R. L. (1980) *The Statistical Analysis of Failure Time Data*. New York: Wiley.

Langsley, D. G., Machotka, P. & Flomenhaft, K. (1971) Avoiding mental hospital admission: a follow-up study. *American Journal of Psychiatry*, **127**, 1391–1394.

Leff, J. & Wing, J. K. (1971) Trial of maintenance therapy in schizophrenia. *British Medical Journal*, *iii*, 599–604.

MECHANIC, D. (1978) Alternatives to mental hospital treatment: a sociological perspective. In *Alternatives to Mental Hospital Treatment* (eds L. I. Stein & M. A. Test). New York, London: Plenum Press.

MECHANIC, D. (1987) Correcting misconceptions in mental health policy: strategies for improved care of the seriously mentally ill. *Milbank Quarterly*, **65**, 203–230.

MOSHER, L. R. (1983) Alternatives to psychiatric hospitalization: why has research failed to be translated into practice? *New England Journal of Medicine*, **309**, 1579–1580.

MOSHER, L. R. & MENN, A. Z. (1978) Community residential treatment for schizophrenia: two-year follow-up. *Hospital and Community Psychiatry*, **29**, 715–723.

NATIONAL INSTITUTE OF MENTAL HEALTH (1986) *Mental Health, United States, 1985*. In DHHS publication no. (ADM)86-1378 (eds C. A. Taube & S. A. Barrett). Washington DC: Supt of Docs, US Govt Printing Office.

—— (1987) *Mental Health, United States, 1987*. In DHSS publication no. (ADM)87-1518 (eds R. W. Manderscheid & S. A. Barrett). Washington, DC: Supt of Docs, US Govt Printing Office.

OKIN, R. L. (1985) Expand the community care system: deinstitutionalization can work. *Hospital and Community Psychiatry*, **36**, 742–745.

REDICK, R. W., WITKIN, M. J., BETHEL, H. E., *et al* (1985) *Trends in Patient Care Episodes in Mental Health Organizations, United States, 1970–1981*. Mental health statistical note no. 171. Rockville: US Department of Health and Human Sciences.

STEIN, L. I., TEST, M. A. & MARX, A. J. (1975) Alternative to the hospital: a controlled study. *American Journal of Psychiatry*, **132**, 517–522.

SUCHMAN, E. A. (1967) *Evaluative Research. Principles and practice in public service and social action programs*. New York: Russel Sage Foundation.

TALBOTT, J . A. (1985) The fact of the public psychiatric system. *Hospital and Community Psychiatry*, **36**, 46–50.

TEN HORN, G. H. M. M., GIEL, R., GULBINAT, W. H. & HENDERSON, J. H. (1986) *Psychiatric case registers in public health*. Amsterdam/New York: Elsevier.

TEST, M. A. & STEIN, L. I. (1978) Training in community living: research design and results. In Stein L. I., Test M. A. (eds.) *Alternatives to Mental Hospital Treatment* (eds L. I. Stein & M. A. Test). New York, London: Plenum Press.

WING, J. K. & FRYERS, T. (1976) *Psychiatric Services in Camberwell and Salford. Statistics from the Camberwell and Salford psychiatric registers, 1964–1974*. London: MRC Social Psychiatry Unit; and Manchester: Department of Community Medicine.

WING, J. K., COOPER, J. E. & SARTORIUS, N. (1974) *Measurement and Classification of Psychiatric Symptoms*. Cambridge: Cambridge University Press.

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The Functional Discrimination of Attachment and Affiliation
Theory and Empirical Demonstration

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Volunteer college students completed a categorisation task designed to test the hypothesis that adults organise their expectations of relationships in a manner that reflects a functional distinction between attachment and affiliation. Terms associated with the provision of security and with characteristics theoretically identified as definitive of attachment relationships were significantly more likely to be associated with the relationship identified as 'lover'. There was substantial overlap between attachment and affiliation relationships in functions relating to intimacy and disclosure. These results highlight the need to differentiate close relationships by functional rather than structural characteristics.

The literature on social support acknowledges attachment to be an important component of adult social networks. For example, Troll & Smith (1976) cited studies providing evidence that "particularized attachments may persist throughout life". Rutter (1981) wrote, "deep attachments and loving bonds are an important feature of adult life". Ainsworth (1985) has stated that "the most important elements in social networks and social support systems alike are relationships that constitute affectional bonds, and particularly those with attachment components that provide a sense of security".

Most of the literature on social support uses attachment, either explicitly or implicitly, to denote the upper range of the affiliative spectrum within social networks. Attachment is assumed to arise from the same needs as other close social relationships, to fulfil the same functions, and to be maintained by the same types of behaviour, cognitions, and affects. The underlying thesis in this paper is that, although attachment and affiliative relationships may serve similar important needs for intimacy and support, only attachment relationships provide the sense of security that is crucial to buffering the effects of stressful life events. The specific hypothesis tested here is that adults organise their expectations of relationships in a manner that reflects this functional distinction.

The study of attachment began with John Bowlby (1969/82, 1973, 1980). Influenced by the findings of ethologists such as Lorenz (1931) and Harlow (1958), Bowlby (1969/82) proposed that attachment is a primary, biologically determined behavioural system in many species, including man, with the function of protecting the altricial animal from danger. The goal of attachment is to maintain or re-establish proximity to an identified protector. Attachment behaviour is "any form of behavior that results in a person attaining or retaining proximity to some other differentiated and preferred individual, who is usually conceived as stronger and/or wiser" (Bowlby, 1977).

Most attachment research has focused on infant–parent relationships. Henderson (1977) is one of the few investigators to attempt a systematic research study that takes into account adult attachment relationships. Henderson stated (in agreement with Caplan, 1974) that "'psychosocial supplies' [are] the essential commodity that people obtain from their social network". He further proposed that an individual has "affective attachments" towards members of his/her primary group and "it is from them that his psychosocial supplies are said to be derived".

Henderson's approach to adult attachments appears, therefore, to define attachment relationships as a subset, identified by intensity and intimacy, of an individual's social support or affiliative network. Similarly, Heard & Lake (1986) have said:

> "'Preferred relationships' refers to relationships in which individuals regularly expect to find opportunities for companionable and/or supportive interactions. . . . People who are so classed constitute an individual's attachment network. . . . The concept of preferred relationships in the attachment network circumvents difficulties in describing attachment relationships and affectional bonds in adults."

There are two implicit assumptions in this approach: (a) attachment can be characterised using the same criteria as affiliation (for example, if affiliative relationships provide companionship and intimacy, attachment relationships provide preferred or more salient companionships and intimacy); and (b) attachment and affiliation serve the same function(s), with attachment, again, doing the job more and better (West & Sheldon, 1987). Neither of these assumptions agrees with theoretical formulations about the nature of the attachment system in infancy and childhood.

In a cogent article, Weiss (1982) characterised attachment relationships for adults. First, he delineated the following three central criteria for defining an attachment relationship in infancy: (a) proximity-seeking – "The infant will attempt to remain within protective range of the attachment figure"; (b) secure base – "In the presence of an attachment figure, so long as there is no threat, an infant will give indication of comfort and security"; and, (c) separation protest – "Threat to continued accessibility to the attachment figure or actual separation . . . will give rise to protest and to attempts to ward off the attachment figure's loss or to regain the attachment figure's presence". Based on evidence from interview studies, Weiss stated that relationships "that meet the three criteria for attachment are to be found regularly" in adults.

Weiss then delineated three characteristics which differentiate attachment in adults from attachment in children. (a) In adults, attachment relationships are typically between peers, rather than between care-receiver (infant) and care-giver (parent). (b) Unlike infant attachment, adult attachment does not normally overwhelm "other behavioral systems" such as the exploratory system. (c) Attachment in adults often includes a sexual relationship.

Finally, Weiss differentiated attachment from other social relationships. This differentiation is based largely on the effects of the absence of different types of bonds. In the absence of an attachment bond, Weiss observed that individuals experienced persistent 'loneliness' which was not relieved by participation in a friendship network. In contrast, individuals "without access to a community of others" experienced distress associated with isolation. In Weiss' terms:

> "What they lacked might be characterized as 'affiliation' – associations in which shared interests and similarity of circumstances provided a basis for mutual loyalty and a sense of community."

This 'affiliation' need is thus congruent with both the 'psychosocial supplies' (Caplan, 1974) provided by the social network and with the exploratory behavioural system which Bowlby (1977) characterised as 'antithetical' to the attachment system.

The study of adult attachment and affiliative relationships, and especially of discrete attachment patterns among adults, presents empirical as well as theoretical challenges. The identification of attachment patterns in infancy and early childhood relies on the structured observation of *behaviour* in attachment-eliciting situations (Ainsworth *et al*, 1978). Researchers such as Ainsworth & Bell (1970) and Hinde & Spencer-Booth (1970) have characterised attachment bonds in human and other primate infants through systematic observation of specific types of behaviour for maintaining proximity (e.g. clinging), re-establishing proximity (e.g. reaching), protesting separation (e.g. crying), and demonstrating pleasure in reunion (e.g. smiling). The infant and young child have relatively limited behavioural repertoires physiologically available, restricted environments of action and, at most, brief stores of past experiences to contribute expectations and learned responses. The relationship between behaviour, behavioural system, and system goal is therefore relatively linear and proximate.

The evaluation of adult attachment relationships is more complex. Adult behaviour typically has multiple determinants, arising from and serving the needs of more than one behavioural system (Bretherton & Ainsworth, 1974; Hinde, 1975; Bateson, 1976). No behaviour is exclusively an attachment behaviour, and relationships may serve more than one function (Sroufe & Waters, 1977; Hinde, 1982). For example, in Western culture, it is a common expectation that one's spouse may also be one's confidante or 'best friend', thereby confounding attachment and affiliative functions. This is congruent with the findings of the Camberwell study, where Brown *et al* (1975) rated 'intimacy' on a four-point scale (a–d). Type a and type b relationships were both defined as "close, intimate, and confiding". Type a relationships were with "husband or boyfriend, or in exceptional cases a woman with whom they lived". Type b relationships were with "mother, sister or friend whom they saw at least weekly". Only type a relationships provide "almost complete protection" against psychiatric sequelae to stressful life events; type b relationships "failed to provide even relative protection".

While the authors admit they cannot explain this difference, attachment theory provides an explanation. In the absence of a stressor causing decreased security, type a and type b relationships fulfil similar affiliative needs equally well. But when a stressor activates the attachment system, attachment needs (the need to re-establish a sense of security) predominate. Only type a relationships have predominant attachment components and thus fulfil attachment needs. The shared residence evokes the secure base hallmark of attachment relationships in infancy. The findings of the Camberwell study can, therefore, be understood as differentiating the attachment from the affiliative components of close relationships.

A further complication in the assessment of adult attachment is that observed attachment patterns in adults arise primarily from set 'representational models' rather than from current environmental stimuli (Bowlby, 1977; Main *et al*, 1985). Findings from another prominent study can be understood in this context. Henderson *et al* (1981) found that the availability of attachment and the perceived adequacy attachment could be reliably differentiated, and that perceived adequacy was more strongly correlated with adjustment following stressful life events than simple availability. These results can be understood as supporting Bowlby's observation (1977) that adult attachment patterns arise largely from:

> "representational models of attachment figures and of self [which] an individual builds during his childhood and adolescence, [and which] tend to persist relatively unchanged into and throughout adult life. As a result he tends to assimilate any new person with whom he may form a bond . . . to an existing model . . . and often to continue to do so despite repeated evidence that the model is inappropriate."

An individual's representational model would thus have greater influence on his or her perception of the adequacy of attachment than objective environmental supplies (i.e. availability).

Finally, although all attachments are affectional bonds, not all affectional bonds are attachments (Ainsworth, 1985). As implied in the above discussion of the Camberwell study, relationships can look equivalent when classified only according to affectional components but can nonetheless be quite different in terms of the ability to fulfil attachment functions. In accordance with the implications of Bowlby's theory (1978), attachment is restricted to dyadic relationships in which proximity to a special 'other' is sought or maintained to provide a sense of security. The principal function of adult attachment is protection from danger (as it is during childhood), although adults recognise other dangers than those recognised by infants and children: specifically, threats to the individual's self-concept and integrity (Hinde, 1975; West *et al*, 1986). Affiliative relationships have a quite different function, serving to promote exploration and expansion of interests from the secure base provided by attachment.

The present study was designed to investigate whether adults organise their expectations of relationships in a manner that reflects a functional distinction between attachment and affiliation.

Method

The study consisted of a simple paper-and-pencil categorisation task. The functions of relationships were operationalised through 45 terms (descriptors) used in the literature to describe attachment, affiliation, and social relations. These relationships were differentiated according to the three primary types: 'lover' was used to denote an attachment relationship, 'best friend' to denote an affiliative relationship, and 'friend' to denote a social relationship. Instructions to subjects stated that the category 'lover' included a person identified as someone the subject is 'in love with', whether or not there is a sexual relationship. Each subject was asked to categorise each descriptor as to whether it applied primarily to 'lover','best friend', or 'friend'. The endorsement of more than one category for each descriptor was allowed.

Subjects

Subjects were 90 volunteer participants from an undergraduate psychology course at the University of Calgary. Although this is a non-random sample, it is especially suited to this investigation for two reasons: (a) the subjects have comparable levels of reading skills, and they could understand the task fairly easily; (b) most subjects were 19–25 years old. This age range is desirable because most subjects will have formed specific ideas about types of relationships, but these ideas will not ordinarily have been greatly modified by contradictory environmental responses. That is, the subjects' ideas about the functions of different types of relationships should reflect generalised expectations (i.e. representational models) at least as much as practical experience.

The questionnaires were anonymous, and only age and sex of respondents were requested. Two returns were discarded because most descriptors had not been categorised. Of the remaining 88 returns, seven did not give age or sex. The 81 returns coded for age and sex included 55 women, aged 22.9 ± 6.8 years, and 26 men, aged 20.6 ± 3.6 years. This age difference was not significant by *t*-test.

Data analysis

The operationalised null hypothesis was "No terms will be preferentially endorsed by most subjects for 'lover' only". Since the data are categorical, the analyses focused on descriptive and non-parametric statistics. First, the descriptors were classified according to modal response category, that is, any descriptor most frequently endorsed as applying to 'lover' only was accepted as a function of attachment relationships. Descriptors most frequently endorsed as applying to both 'lover' and 'best friend' were accepted as common to both attachment and affiliative relationships.

The non-parametric Kruskal–Wallis procedure was used to test for statistically significant differentiation of attachment and affiliative functions (Rosner, 1986). The test was performed on the number of subjects endorsing only the 'lover' category for each descriptor. Those descriptors with a modal response category of 'lover' were identified as group 1; all other descriptors were identified as group 0. The Kruskal–Wallis test ranks all observations, and tests the null hypothesis that the centre of group 0 equals the centre of group 1. The test statistic, H, follows

TABLE I
Descriptors assigned to attachment relationships

Descriptor	*No. endorsing 'lover' only*	*Mode = 'lover' only*
Sexual intimacy	83	Yes
Plan future with	63	Yes
Exclusive	59	Yes
Separation causes distress	56	Yes
You protest separation from	56	Yes
Other's happiness is a goal for you	50	Yes
Opportunity to give nurturance	45	Yes
Provides sense of being needed	40	Yes
Provides sense of security	40	Yes
Care giver	34	Yes
Faithful	33	Yes
You fear loss of	29	No
You protect	25	No
Permanent relationship	24	No
Sought out when stressed	21	No
Enduring tie	21	No
Prevents loneliness	18	No

a χ^2 distribution with degrees of freedom equal to one less than the number of groups (i.e. for this study, d.f. = 1).

Because we had prior expectations (based on our understanding of the function of attachment relationships for adults) of which descriptors would be preferentially assigned to the 'lover' category only, a Kruskal–Wallis test was also done with the descriptors divided into two groups based on expected association with attachment. The first column of Table I lists the 17 descriptors we predicted would be uniquely associated with the 'lover' category.

Results

Two related descriptors ('fixed and complementary' and 'variable and equivalent') were discarded from the analysis as most subjects either ignored them or indicated confusion as to their meaning. Only four modal response categories were observed for all 43 remaining descriptors.

Nine descriptors were endorsed most frequently either for 'friend' only or for all three categories. These patterns of endorsement are interpreted as indicating functions assigned to general social relationships. The nine terms are: 'shares common interests', 'competitive at times', 'independent', 'provides companionship', 'helps you to be sociable', 'prevents loneliness', 'prevents isolation', 'co-operative', and 'comfortable'. The association of these functions with general social relationships has a face validity that lends credence to the general approach.

Twenty-three descriptors were endorsed most frequently for both 'lover' and 'best friend' (Table II). This pattern of endorsement was interpreted as indicating functions assigned to close affiliative relationships. Additionally, this pattern of endorsement indicates the functional overlap between attachment and affiliative relationships in Western culture. The relationship entitled 'lover' is clearly expected to fulfil the same functions as the relationship 'best friend'.

Eleven descriptors were endorsed most frequently for 'lover' only. The null hypothesis was therefore rejected for this sample. All were from the set of 17 descriptors hypothesised to be uniquely associated with attachment (Table I).

For the first Kruskal–Wallis test, groups were identified according to modal response category; only the 11 descriptors with a modal response of 'lover' were identified as attachment descriptors. The descriptors were ranked according to the number of subjects endorsing only the 'lover' category; the 32 non-attachment descriptors had an average rank of 16.5; the 11 attachment descriptors had an average rank of 38.0. The H statistic, adjusted for ties, is 24.07; the cumulative distribution function at 24.07 of χ^2 with d.f. = 1 is 1.0. The null hypothesis of no difference can therefore be rejected ($P<0.001$).

TABLE II
Descriptors associated with affiliative relationships

Descriptor	*No. of endorsements for both 'lover' and 'best friend'*
Mutually confiding	58
Knows a lot about you	58
Mutual trust	47
Wants to maintain closeness	47
Provides you with a sense of worth	44
You cherish	43
Provides reassurance	40
Important as a unique individual	39
Enduring tie	39
Provides guidance and advice	39
Loyal	39
You fear loss of this person	37
Permanent relationship	37
Sought out at times of stress	37
Loss means grief	36
Frequent shared activities	36
Pleasure in reunion	36
Frequently sought out	35
Offers help when needed	30
Shared interpretations	29
You try to protect	27
Predictable	26
Shared activities most important	25

P, 25, 422

The second test assigned all 12 descriptors hypothesised as unique to attachment to the attachment group. The 26 non-attachment descriptors had an average rank of 14.3; the 17 attachment descriptors had an average rank of 33.8. The *H* statistic, adjusted for ties, is 24.88. The cumulative distribution function χ^2 with d.f. = 1 at 24.88 is 1.0. Therefore, the inclusion of all hypothesised attachment descriptors does not decrease the confidence with which the null hypothesis can be rejected.

Because of the large number of subjects who endorsed the item 'sexual intimacy' for lover only, we questioned whether this single item was unduly biasing the results. We therefore repeated both analyses omitting that item. The Kruskal–Wallis test for the ten remaining items with a modal response of 'lover only' versus all other items yielded an *H* statistic, adjusted for ties, of 22.39. The test for the 16 theoretically predicted attachment items versus all others yielded an *H* statistic, adjusted for ties, of 23.66. Both of these values still lead to rejection of the null hypothesis ($P<0.001$).

P values are a component of inferential statistics, indicating the probability of a type I error. As this sample is not a random sample of any population, inferential statistics must be accepted with caution. Inferences from observed findings to the generalised research question must therefore be accepted primarily on logical, not statistical, grounds.

Discussion

The 11 terms endorsed preferentially for 'lover' only compare favourably with the characteristics of adult attachment relationships delineated by Weiss (1982) (see earlier). Two of the characteristics common to infant and adult attachment can be related directly to terms endorsed for 'lover' only: secure base with 'provides sense of security', and separation protest with 'you protest separation from' and 'separation causes distress'. Proximity-seeking does not seem to be strongly associated with adult attachment relationships as the terms 'frequently sought out', 'sought out when stressed', and 'wants to maintain closeness' were each endorsed for both 'lover' and 'best friend'.

One possible interpretation of these results is that affiliative relationships include the expectation of frequent contact but not the expectation that this contact is guaranteed or will necessarily always be available when wanted or in the future. In contrast, the association of the terms 'plan future with', 'faithful' and 'care-giver' with only the 'lover' category suggest that adults expect attachment relationships to provide availability and security not only in the present but also in the future. Thus, expectations of a shared future become a crucial hallmark of adult attachment relationships.

Weiss also identified three characteristics which differentiated adult from infant attachment (see earlier). The peer relationship component is indicated in these results by the expectation of reciprocity: 'other's happiness is a goal for you', 'opportunity to give nurturance' and 'provides sense of being needed', all of which were preferentially endorsed for the category of 'lover' only. The term 'sexual intimacy' indicates the association of a sexual relationship with attachment. (The terms 'exclusive' and 'faithful' could also be interpreted as relating to the sexual component of the relationship.) The third characteristic, decreased ability of the attachment system to overwhelm other behavioural systems, is not directly tested in this study, but can be inferred from the large number of functions assigned to both 'lover' and 'best friend'. The attachment and affiliative systems are not, therefore, antithetical in all functions. One system would not ordinarily be capable of completely overwhelming the other, in that the shared functions, at least, would be maintained.

The results of this study suggest that attachment for adults must be defined for investigation primarily in terms of *function* (protection from 'danger' with achievement of security being the signal that terminates attachment behaviour) rather than in terms of *structure* (specific behaviour or form of relationship or role-defined 'other'). Any relationship may have an attachment component to the degree that the relationship promotes security. A relationship becomes an attachment relationship when the primary function of the relationship is the protection from 'danger'.

The delineation of the functions of attachment versus affiliative relationships could also help clarify the often confusing findings regarding social support and stressful life events. In a longitudinal study of single and non-single mothers in Islington, Brown *et al* (1986) found that the existence of a confiding relationship was *not* associated with a lower risk of depression among wives, but access to socially supportive relationships *was* protective against depression for single mothers. These findings do seem to suggest, at a minimum, that there exist three different kinds of relationships: marital relationships, confidante relationships, and socially supportive relationships. The association between confidants, social support, life events, and onset of depression is apparently different in the presence or absence of what appears to be an attachment relationship. It would appear that the attachment relationship has to be taken into account before the contribution of affiliative relationships, whether intimate or more distant, to buffering stressful life events can be understood.

Bowlby (1988) has recently stated that "the extent to which [each individual] becomes resilient to stressful life events is determined to a very significant degree by the pattern of attachment he or she develops during the early years". Our research suggests that, in adults, these patterns of attachment are best investigated by attention to functional rather than structural differences in relationships and, further, that the essential function of attachment relationships for adults is protection from 'dangers'; the primary signal that this function has been achieved is the sense of present and future security within the relationship.

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References

Ainsworth, M. D. S. (1985) Attachments across the life span. *Bulletin of New York Academy of Medicine*, 61, 792–812.

—— & Bell, S. M. (1970) Attachment, exploration and separation: illustrated by the behaviour of one-year-olds in a strange situation. *Child Development*, 41, 49–67.

——, Blehar, M., Waters, E., *et al* (1978) *Patterns of Attachment*. Hillsdale, New Jersey: Lawrence Erlbaum.

Bateson, P. P. G. (1976) Specificity and the origins of behavior. In *Advances in the Study of Behavior* (eds J. S. Rosenblatt, R. A. Hinde, E. Shaw, *et al*). New York: Academic Press.

Bowlby, J. (1969/82) *Attachment and Loss, Vol. 1: Attachment*. (2nd edn). New York: Basic Books.

—— (1973) *Attachment and Loss, Vol. 2: Separation: Anxiety and Anger*. New York: Basic Books.

—— (1977) The making and breaking of affectional bonds. *British Journal of Psychiatry*, 130, 201–210.

—— (1978) Attachment and loss: retrospect and prospect. *American Journal of Orthopsychiatry*, 52, 664–678.

—— (1980) *Attachment and Loss, Vol. 3: Loss: Sadness and Depression*. New York: Basic Books.

—— (1988) Developmental psychiatry comes of age. *American Journal of Psychiatry*, 146, 1–10.

Bretherton, I. & Ainsworth, M. (1974) Responses of one-year-olds to a stranger in a strange situation. In *The Origins of Fear* (eds M. Lewis & L. Rosenblum). New York: Wiley.

Brown, G. W., Bhrolchain, M. N. & Harris, T. (1975) Social class and psychiatric disturbance among women in an urban population. *Sociology*, 9, 225–254.

——, Andrews, B., Bifulco, A., *et al* (1986) Social support, self-esteem and depression. *Psychological Medicine*, 16, 813–831.

Caplan, G. (1974) *Support Systems and Community Mental Health*. New York: Behavioral Publications.

Harlow, H. F. (1958) The nature of love. *American Psychologist*, 13, 673–685.

Heard, D. H. & Lake, B. (1986) The attachment dynamic in adult life. *British Journal of Psychiatry*, 149, 430–438.

Henderson, S. (1977) The social network, support and neurosis: the function of attachment in adult life. *British Journal of Psychiatry*, 131, 185–191.

——, Byrne, D. G. & Duncan-Jones, P. (1981) *Neurosis and the Social Environment*. Sydney: Academic Press.

Hinde, R. (1975) The concept of function. In *Function and Evolution in Behavior* (eds G. P. Barends, C. Beer & A. Manning). Oxford: Clarendon Press.

—— (1982) Attachment: some conceptual and biological issues. In *The Place of Attachment in Human Behavior* (eds C. M. Parkes & J. Stevenson-Hinde). New York: Basic Books.

—— & Spencer-Booth, Y. (1970) Individual differences in the response of rhesus monkeys to a period of separation from their mothers. *Journal of Child Psychology and Psychiatry*, 11, 159–176.

Lorenz, K. (1931) *Beitrage zur Ethologie sozialer Corviden*. Translated (1970) in *Studies in Animal and Human Behaviour*, vol. I (ed. R. B. Martin). Cambridge, MA: Harvard University Press.

Main, M., Kaplan, N. & Cassidy, J. (1985) Security in infancy, childhood and adulthood: a move to the level of representation. In *Growing Points in Attachment Theory and Research* (eds I. Bretherton & E. Waters). Monograph of the Society for Research, in Child Development, Serial No. 209, 50 (1–2), 66–104.

Rosner, B. (1986) *Fundamentals of Biostatistics* (2nd edn). Boston: Duxbury Press.

Ruttero, M. (1981) Attachment and the development of social relationships. *Scientific Foundations of Developmental Psychiatry* (ed. M. Rutter). Baltimore: University Park Press.

Sroufe, L. A. & Waters, E. (1977) Attachment as an organizing construct. *Child Development*, 48, 1184–1199.

Troll, L. E. & Smith, J. (1976) Attachment through the life span: some questions about dyadic bonds among adults. *Human Development*, 19, 156–170.

Weiss, R. S. (1982) Attachment in adult life. *The Place of Attachment in Human Behavior* (eds C. M. Parkes & J. Stevenson-Hinde). New York: Basic Books.

West, M., Livesley, J., Reiffer, L., *et al* (1986) The place of attachment in the life events model of stress and illness. *Canadian Journal of Psychiatry*, 31, 202–207.

—— & Sheldon, A. (1987) Letter to the editor. *British Journal of Psychiatry*, 150, 408–409.

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Adult Personality Functioning Assessment (APFA)
An Investigator-Based Standardised Interview

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The development of an investigator-based standardised interview to assess patterns of specific and general social dysfunction is described. It covers six domains of functioning: work; love relationships; friendships; non-intimate social contacts; negotiations; and everyday coping. Inter-rater reliability was tested by three investigators rating 21 audiotaped interviews, and was shown to be high, with an intraclass correlation of 0.87 for the total score. The pattern of associations between specific and general social dysfunction was examined through determination of sensitivities and specificities and through LISREL modelling. The findings varied across social domains but it was concluded that the total APFA score provided a reasonable measure of general social dysfunction.

During recent years there has been the development of a range of standardised questionnaire and interview measures of personality disorder as conceptualised in both DSM–III and ICD–9 (Merikangas & Weissman, 1986; Reich, 1985; Tyrer & Ferguson, 1987). In contrast to the poor agreement on the diagnosis of personality disorder generally found between clinicians using non-standardised interviews, several of these standardised techniques have been shown to have fairly good reliability. However, little is known of their validity, and they are limited in being tied to current concepts of personality disorder, which are both contradictory and poorly substantiated (Frances & Widiger, 1986; Rutter, 1987*a*). Those based on ICD–9 (World Health Organization, 1978) approach the diagnosis of personality through the assessment of particular traits represented by such features as dysthmia, aggressivity, and obsessionality (Mann *et al*, 1981; Tyrer *et al*, 1979, 1984). Those based on DSM–III (American Psychiatric Association, 1980) to some extent do the same, but the main emphasis is on particular types of behaviour or states of mind thought to characterise specific personality disorders (Siever & Klar, 1986).

Thus, the diagnosis of antisocial personality disorder is based on consistent violation of the rights of others and lack of loyalty in interpersonal relationships; and that of schizotypal personality disorder on cognitive perceptual distortions and social withdrawal. A problem arises, however, from the finding that the majority of individuals who meet the criteria for one type of personality disorder also meet the criteria for at least one other (Clarkin *et al*, 1983; Mellsop *et al*, 1982; Stangl *et al*, 1985). But the disorders do not overlap randomly; some are closely related to one another whereas others stand out as different both in concept and as measured (Clarkin *et al*, 1983; Rutter, 1987*a*). Probably, those that represent lesser variants of specific psychiatric disorders (such as schizotypal and personality disorder and schizophrenia, or cyclothymic/affective personality disorder and affective disorder) need to be differentiated from the rest. The remainder, although separately defined in terms of particular traits or types of behaviour, have in common a pervasive and persistent abnormality in social functioning. However, none of the existing interview assessments of personality disorder focuses on this as a central feature.

Social functioning has been the focus of the 30 or so scales measuring various aspects of social adjustment. These have been systematically reviewed by Weissman and her colleagues (Weissman, 1975; Weissman *et al*, 1981; John & Weissman, 1987), and an additional interview measure of social role performance has been described by Sturt & Wykes (1987). A range of useful measures is available, many of which have been shown to have satisfactory psychometric properties, but none is intended to assess personality functioning (and could not do so without a major reorientation). Rather, most were designed to evaluate patients' community adjustment either while ill or following recovery. Accordingly, the focus is on the present (rather than lifetime) and on the impact of illness, often with measures of satisfaction and subjective feelings. Most of the scales follow a highly structured questionnaire format, with the limitation that many items apply to only some subjects and that scoring procedures do not take into account the person's social context or situation (Katschnig, 1983).

Thus, existing measures that might be used to assess personality functioning tend to concentrate on either temperamental traits and supposedly specific psychological abnormality, or on aspects of current social adjustment and satisfaction. Neither group of measures provides an adequate evaluation of objectively defined social functioning in a range of domains. Such an evaluation is required if personality disorder is conceptualised as requiring a pervasive and persistent abnormality in social functioning. However, in the present state of knowledge, it is necessary that the measurement should not be tied to any one classification scheme (Rutter & Pickles, 1989). Not only do we lack data on the links between social malfunction and deviant temperamental traits or specific psychological abnormalities, but also it is not known how commonly individuals have persistent abnormalities in some social domains but not in others. The question of how pervasive social malfunction must be for personality disorders to be diagnosed requires empirical data as much as theory, if it is to be answered satisfactorily.

Moreover, it is clear that many individuals are likely to show malfunction in particular social domains or in particular situations for reasons that are separate from personality disorder. Thus, often, marital problems will be a function of difficulties in that particular dyadic relationship, or there may be a pervasive difficulty in intimate relationships that is a consequence of, say, insecurities in attachment relationships in childhood, but which is not accompanied by any problems in work or everyday coping.

It seems therefore that what is needed, but what has been lacking, is a standardised measure of a person's functioning over time in a range of different social domains, the measurement being done in a way that can deal with varied life circumstances and which can assess functioning in people without, as well as with, acute psychiatric disorder. The Adult Personality Functioning Assessment (APFA), a standardised investigator-based interview, was designed to fill that gap. In this paper we describe its rationale and format and give findings on its reliability and structure as assessed on the subject version of the interview.

The Adult Personality Functioning Assessment

The interview is primarily designed to provide a standardised assessment of a person's functioning in a range of social domains, with the aim of both identifying dysfunction that is specific to particular domains and measuring general social dysfunction that is pervasive across most social domains. Six domains were selected as representative of the variety of social demands likely to be faced by most people regardless of their circumstances. These are: work; love relationships; friendships; non-intimate social contacts; negotiations; and everyday coping. In each domain, the intention is to determine the person's level of functioning regarding role performance in that domain, without reference to functioning in other social domains.

Rating of level and type of functioning

For each domain, the rating of level of functioning is made on a six-point scale extending from '0' (*unusually effective in the operative life circumstances* to a degree that is clearly above average to a substantial degree) to '5' (pervasive failure of role performance in the specified domain). The latter would apply, for example, in work if the subject had failed to hold any job for more than brief periods; and in love relationships if there were an absence of sustained committed relationships or if marriage/cohabitation were maintained only in the face of open hostility or apathy leading to essentially separate lives.

The process of rating necessarily involves the weighing up of a complex mixture of different aspects of functioning, with the need to balance elements of successful role performance against elements of role failure. Comparability is ensured by four features. First, for each domain there is explicit specification of the elements to be taken into account and how they are to be combined. For example, the rating for 'work' requires attention to conflict with supervisors or fellow-workers, difficulties resulting from poor work performance, frequent changes of job, absences from work, poor time-keeping, and being sacked or walking out from a job. Similarly, the rating for 'non-intimate social contacts' takes into account the frequency, range, and nature of interactions with neighbours and acquaintances and participation in social situations, with particular reference to altercations with people, or avoidance of social participation, or marked circumscribing of topics of conversations with others. These features are summarised in the interview schedule and are outlined in greater detail in the manual that accompanies it (not published here, but both are available at cost price from the authors). Secondly, a 'dictionary' of examples accumulated from the use of the interview in several studies provides details of how various combinations of features should be rated. Thirdly, the schedule provides explicit guidance on the topics to be covered, together with a listing of suggested probes.

Thus 'negotiations' requires an account of the subject's performance in commercial and professional transactions with people outside the family. The interviewer is required to ask about fairly routine negotiations such as making purchases in a shop or making an appointment at the doctor or dentist; those involving some explanation and assertion of rights, such as applying for a job or taking an unsatisfactory item back to a shop or discussing a child's progress with teachers; and those that require a point of view to be put with some persistence, as with the failure of a landlord to undertake essential repairs or where there has been a major difference of opinion over some aspect of a child's education. Similarly, everyday coping refers to the responsibility taken for tasks in the home such as cooking meals, washing, looking after children, keeping the house in good order and managing the finances. Unlike the other five domains, this does not involve interpersonal skills.

Fourthly, a step-by-step strategy is followed in rating. The first decision is whether there is substantial dysfunction in the domain; if there is, the rating must be 3, 4 or 5; if not, the rating must be 0, 1 or 2. Ordinarily, any serious dysfunction requires a rating of '3' or worse. Thus, someone who had had temporary marital separations through discord or who had lost several friendships as a result of quarrelling or some kind of rift would rate '3' unless there were some special circumstances. If there is not substantial dysfunction, the next decision is whether the functioning is more than adequate in showing markedly positive features without any significant negative ones. A rating of '0' on love relationships would require not only temporal stability but positive trust, marked confiding and enjoyment. A '1' rating is made where functioning is generally satisfactory and without significant lasting difficulties, but lacking the positive features required for '0'. A '2' rating implies that the level of functioning is mostly satisfactory but there are significant difficulties of one kind or another. The differentiation between 3, 4 and 5 is based on the seriousness of the dysfunction, its extensiveness over situations, and the presence/absence of aspects of good functioning. Thus, a rating of '3' on 'love relationships' might be appropriate if the predominant pattern were one of tension and discord but yet there were some shared activities and a degree of commitment.

For each domain, a separate rating is made of the type of dysfunction. The main differentiation is between dysfunction characterised by arguments, discord, tension, aggression or violence, and that mainly characterised by apathy, lack of involvement or avoidance, but there is also provision for rating 'other' types.

Period of coverage and applicability

People's social circumstances and role performance requirements are likely to vary greatly over the life span and if levels of social performance are to be used in assessing personality functioning, it is necessary to specify which age period is to be used in rating. APFA ordinarily uses the 21–30 year period as a baseline (but provision is made for circumstances in which some other age period has to be used). Three particular considerations must be taken into account in assessing the subject's psychosocial functioning: opportunity, circumstances, and association with illness or psychiatric disorder. Functioning can be assessed only if the person has had the opportunity to function in the specified domain. The domains and age period were chosen to ensure that the great majority of people will have had the necessary opportunities but this will not always be the case (as, for example, when someone has been in prison) and the manual provides guidance on how to deal with this issue. The general principle is that performance should be rated only for time periods when opportunities have been present but that there should be detailed questioning to determine whether the lack of opportunity was a consequence of personal social dysfunction (for example, whether unemployment was a consequence of redundancy or dismissal or failure to seek work). In cases in which ratings on one domain are not applicable through lack of opportunity, scores for the other domains may be prorated to derive a total score. Similar issues arise with respect to circumstances. Ratings for each domain are based on the level of functioning relevant to the circumstances that the subject is in, but the interviewer is required to question in detail to determine how the circumstances arose and whether they were a consequence of the person's own performance.

Most current concepts of personality functioning require that the assessment applies to periods that are free of acute psychiatric disturbance. This expectation is based on the need to differentiate habitual levels of functioning from those that are impaired as a consequence of, say, an episode of depression or an obsessional state. However, this distinction is not always straightforward in practice and it is by no means free of theoretical objections (Docherty *et al*, 1986). Thus, some forms of personality disorder are characterised by recurrent episodes of affective disturbance (this would apply, for example, to so-called borderline personality disorders – Tarnopolsky & Berelowitz, 1987); and others are thought to arise out of, or to constitute part of, a chronic psychiatric condition (as, for instance, with schizophrenia). The empirical testing of associations between personality disorders and other psychiatric conditions is possible only if assessments of both are undertaken separately and if personality functioning is rated both during and apart from episodes of psychiatric disorder. That is the procedure followed by APFA. The interview is designed to be preceded by a lifetime assessment of psychiatric disorder so that periods of functioning that have been accompanied by significant symptomatology can be identified. In our studies we have used a modified version of the SADS–L (Harrington *et al*, 1988).

Interview style

APFA is an investigator-based standardised interview (Brown & Rutter 1966; Graham & Rutter, 1968; Le Couteur *et al*, 1989; Rutter & Brown, 1966). This means that ratings are made by the *interviewer* on the basis of descriptions of behaviour. This contrasts with respondent-based interviews in which ratings are essentially based on whether the *informant* says 'yes' or 'no' to specified questions that ask about particular types of behaviour. The latter work well when there is general agreement on the concept involved but are unsatisfactory when lay and professional concepts differ or where the concept is complex and in need of detailed specification (Breslau, 1987). The advantage of an investigator-based approach in these circumstances is that interviewers can be trained to ensure that the concepts are fully understood and that the codings can provide detailed instructions on what should be taken into account. In this way, it is possible to provide a high degree of structure and operationalisation, but with the structure residing in specification to the interviewer of the concept and coding rather than in specification to the informant of the wording of individual questions. However, for this to be possible it is essential that the concepts be made explicit in the interview schedule and accompanying manual, as they are for APFA, and that interviewers be adequately trained in both the techniques of interviewing and the rules and concepts governing the ratings.

The interviewer's task is to obtain detailed descriptions of the subject's role and activities in specified situations. The onus is on interviewers to use their knowledge of the concept and of the respondent's particular situation to adapt the questions to provide the necessary search for the required information. The ratings in all cases are based on descriptions of behaviour and *not* on affirmative or negative answers to closed questions. Moreover, it is behaviour that is relevant and not attitudes, cognitions or self-concepts. Thus, it is irrelevant whether the subject views him or herself as an effective negotiator or as a good worker or as shy or socially incompetent. Such statements provide the cue to ask for examples of how that is shown, but it is the behaviour and not the attitude that is rated.

Method

Two studies on the qualities of APFA were undertaken:

(a) an inter-rater reliability study, and
(b) an investigation of patterns of malfunction in the different social domains as they related to the hypothesised psychological construct of personality disorder.

Sample

In order satisfactorily to investigate the properties of APFA, it was necessary to have a sample that provided a good spread on quality of social functioning with an adequate number of individuals with pervasive social dysfunction. It was also desirable that the sample covered a wide range of social circumstances in order to test whether the instrument could provide comparable measures when people's living conditions varied greatly. To meet these needs, a sample was constructed from four separate sources. First, there were 40 parents (21 men and 19 women) of children currently attending a psychiatric clinic (the Maudsley Hospital). This is known to be a group with a relatively high rate of psychiatric disorder, often involving chronic social dysfunction (Rutter, 1966, 1987*b*). Second, there were 18 individuals (8 men and 10 women) *currently* attending the adult out-patient department of the same hospital for some non-psychotic disorder involving social difficulties. Third, there were 24 individuals (14 men and 10 women) who were part of a follow-up into adult life of people previously treated for psychiatric problems in childhood. Again, this is a group for which previous research has shown a high rate of psychopathology in adult life (Robins, 1966, 1978; Rutter, 1984). Fourth, there were 15 parents (6 men and 9 women) of these *ex*-patients. In all, this constituted a sample of 97 subjects, of which 49 were male and 48 female.

For some purposes, it was desirable to separate those who were being treated for psychiatric problems in their own right, or who had been so treated in the past. This subgroup was termed 'patients' and was made up of the second and third sources; a total of 42 (22 men and 20 women), with a median age of 31 years (range 24–66). The second subgroup, termed 'parents', comprised the parents of child patients and the parents of ex-child patients, i.e. the first and fourth sources. There were 55 'parents' in all (27 men and 28 women) with a median age of 43 years (range 19–76). Of the total sample, 66 were currently married or cohabiting. Of the remaining 31, 17 had been married previously or had cohabited for at least 6 months. Of the

97, 25 had a current psychiatric condition other than personality disorder (assessed on the basis of a SADS-L interview – see Harrington *et al*, 1988) and a further 48 had had such a condition at some time in the past. For obvious reasons, all the subjects who had never had any psychiatric disorder were in the 'parent' group.

Reliability study

For the reliability study, 21 audiotaped interviews were each rated independently by HF, RH and JH (i.e. each interview was rated three times). These 21 interviews comprised 7 interviews by each of the three investigators, which were randomly selected from the 58 interviews from the first two sources (current adult out-patients and parents of current child patients). The sample included 12 men and 9 women, with ages ranging from 26 to 66 years.

The APFA is designed to assess social dysfunction both in relation to specific domains such as work or marriage, and in relation to the hypothesised construct of general dysfunction usually conceptualised as personality disorder. Accordingly, intraclass correlations (Bartko & Carpenter, 1976) were calculated separately for each domain and for the total score (i.e. the sum of the scores for each of the six domains). A particular issue regarding reliability concerns the possible tendency for some interviewers consistently to rate higher or lower than others. This was examined by comparing the mean APFA scores for the three raters, using a one-way analysis of variance.

For each of the social domains, a categorised rating of the type of dysfunction was made (no malfunction, predominant discord/breakdown, predominant avoidance/apathy, and other). For these categorical ratings, inter-rater agreement was assessed using the kappa statistic (Cohen, 1968).

Analysis of patterns of dysfunction

The analysis of patterns of social dysfunction was undertaken on the total sample of 97, but also with separate analyses on groups disaggregated according to patient/parent status and to sex. As already noted, APFA was devised to assess both dysfunction in specific social domains and also generalised social dysfunction. It was assumed that both would occur. Thus, for example, in some cases, individuals with major marital problems will have difficulties that are specific to intense, intimate cohabiting relationships, whereas in other cases the marital problems will form part of a more pervasive pattern of social dysfunction. Accordingly, it was necessary to determine the extent to which the measures for each of the six domains reflected generalised dysfunction – operationally defined as a total APFA score of 16 or greater. This cut-off was chosen because, in order to reach such a score, a person must have had major problems in at least two domains and is likely to have major problems in at least three or four. For this purpose, 'major problems' was defined as a domain subscore of at least 3 (meaning major problems but some significant positive functioning). The value of each domain subscore as a reflection of generalised social dysfunction was assessed in two separate ways. First, the sensitivity and specificity of each subscore were assessed. In this connection, sensitivity constitutes the rate of abnormal subscores in individuals *with* generalised dysfunction; and specificity is the rate of non-abnormal subscores in individuals *without* generalised dysfunction. Second, the confirmatory factor analysis approach of LISREL (Joreskog & Sorbum, 1981) was used to fit a model of a single latent variable of generalised social dysfunction to the data.

Results

Inter-rater reliability

The intraclass correlation coefficients between the three raters for scores on the six separate social domains and for the total APFA score are shown in Table I. Four out of the six domains showed overall correlations that exceeded 0.75, the exceptions being negotiations and everyday coping with correlations of 0.69 and 0.60 respectively. Over the scales as a whole, the raters disagreed by as much as 2 points (on a 6-point scale) in only 6% of cases. It seemed that the somewhat lower, although still acceptable, reliability for the negotiations and everyday coping scales was a function of the rather greater judgement required in rating social functioning in these areas. These two scales also showed the lowest proportion of abnormal scores (28% and 24% respectively versus 30% for work, 57% for love relationships, 47% for friendships, and 37% for non-intimate social contacts in the total sample of 97). The intraclass correlation for the total APFA score was 0.87, with the correlations for individual pairs of raters ranging from 0.85 to 0.90. Agreement between raters on the categorical measure of generalised social dysfunction, operationally defined as a total APFA score of 16 or greater, was also high. There were only three disagreements out of a total of 63 paired comparisons, yielding a kappa value of 0.88.

TABLE I

Agreement between raters 1, 2, and 3 on the score in each social domain and on the total AFPA score (21 subjects)

Social domain	*Rater pairs (ICC*[1]*)*			*All 3 raters*	
	1,2	*1,3*	*2,3*	*ICC*	*Lower 95% CL*[2]
Work	0.74	0.77	0.77	0.76	0.61
Love relationships	0.83	0.79	0.84	0.81	0.68
Friends	0.81	0.76	0.93	0.84	0.73
Non-intimate social contacts	0.89	0.88	0.91	0.89	0.81
Negotiations	(0.64)	0.78	(0.65)	0.69	0.51
Everyday coping	(0.54)	(0.65)	(0.63)	0.60	0.40
Total score	0.85	0.88	0.90	0.87	0.78

1. Intraclass correlation coefficient.
2. Lower 95% confidence limit (for all 3 raters).

All intraclass correlation coefficients were significant at $P < 0.001$ except where bracketed, when $P < 0.01$.

The three raters were also generally similar in their level of rating. Thus, the mean total APFA scores for the three raters were 12.4, 12.2 and 12.6, the differences between them falling short of statistical significance on a one-way analysis of variance.

For each social domain with a level rating of 2 or worse, a rating was made of the type of dysfunction (whether discordant or avoidant). The number of ratings was too low to assess reliability separately for each domain (because too many ratings of level of dysfunction were '0' or '1'); accordingly kappa values were calculated pooling the ratings for the six domains. The inter-rater reliability kappas for the three pairs of raters were 0.74, 0.67 and 0.69.

Distribution of scores

There are two different ways in which APFA scores may be used to derive a measure of general social dysfunction. First, the scores of the six separate social domains may be summed to produce a total score with a range from 0 to 30. Second, a count may be made of the number of domains showing major dysfunction (operationally defined as a score of three or greater). Figure 1 shows the distribution of scores for the total sample of 97 according to the first method, and Fig. 2 according to the second method. In this sample of subjects, deliberately weighted to include a relatively high proportion with long-standing psychiatric problems, the modal total score was 10–12, meaning that the average score for each domain showed adequate functioning, but with some problems. Over half the sample (54/97) had scores of 12 or less. Conversely, a third (32/97) had scores of 16 or greater, meaning that there must be major problems in at least two social domains. The picture obtained from looking at the number of domains with major problems (Fig. 2) is broadly comparable. Nearly half (46/97) the sample showed major

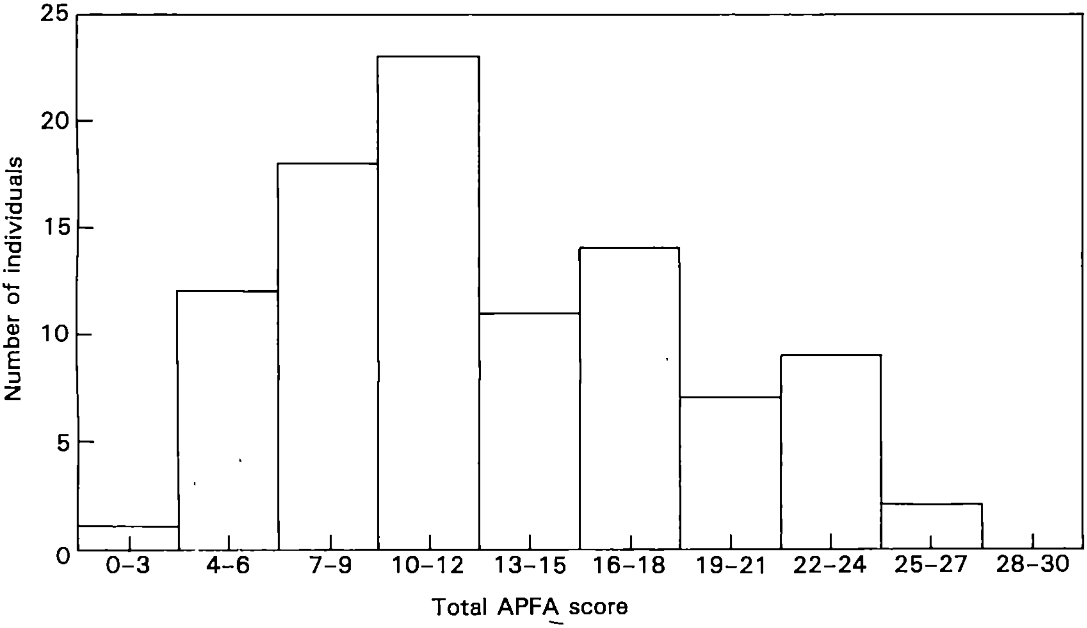

FIG. 1 Distribution of total APFA scores in the whole sample ($n = 97$)

TABLE II
Patterns of social dysfunction: mean (s.d.) domain score according to patient/parent status and according to male/female status

	Work	*Love relationships*	*Friendships*	*Non-intimate social contacts*	*Negotiations*	*Everyday coping*	*Total score*
Patients ($n = 42$)	2.3 (1.4)	3.3 (1.4)	2.6 (1.3)	2.5 (1.3)	2.0 (1.0)	2.2 (1.2)	15.0 (5.9)
Parents ($n = 55$)	1.4 (1.0)	2.5 (1.3)	2.1 (1.4)	1.9 (1.2)	1.8 (1.2)	1.5 (1.0)	11.2 (5.3)
Men ($n = 49$)	1.9 (1.4)	2.8 (1.5)	2.5 (1.4)	2.5 (1.4)	2.1 (1.2)	2.0 (1.1)	13.9 (6.2)
Women ($n = 48$)	1.7 (1.1)	2.8 (1.3)	2.1 (1.3)	1.9 (1.2)	1.7 (1.0)	1.5 (1.1)	11.8 (5.3)

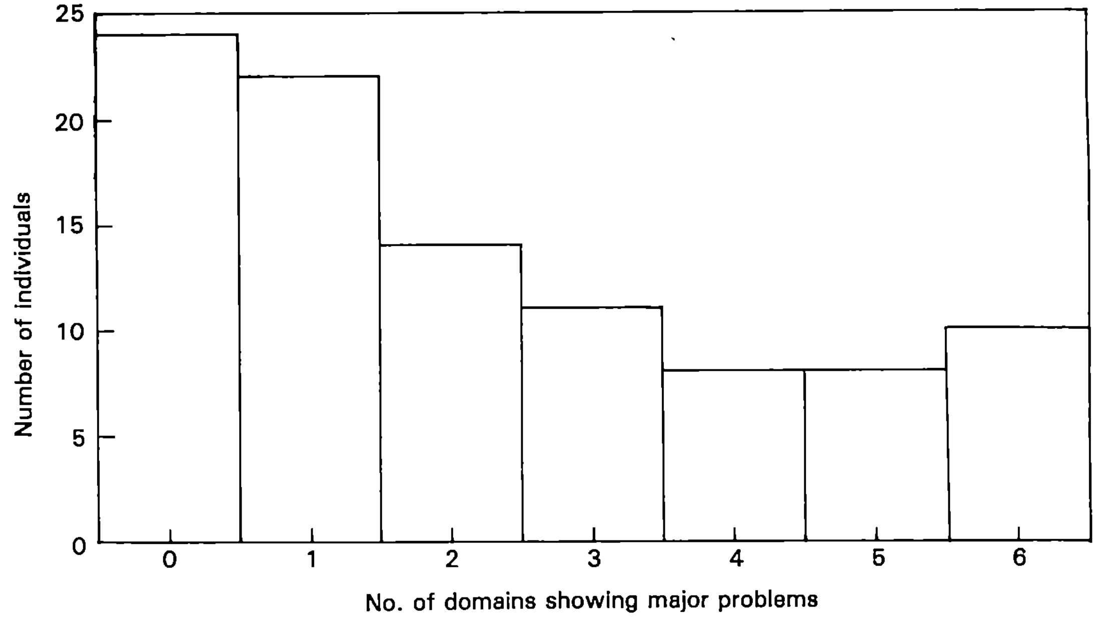

FIG. 2 Distribution of spread of dysfunction across social domains ($n = 97$)

problems in only one domain or less, whereas over a quarter (26/97) showed major problems in at least four domains. Not surprisingly, the two approaches tended to pick out the same individuals. All the subjects with major problems in at least four domains had a total APFA score of 16 or greater and of the 32 subjects with a total score of 16 or more, 26 showed major dysfunction in at least four domains.

Table II shows the total scores and separate social domain subscores for patients/ex-patients compared with parents, and for men compared with women. As expected, the mean total score for the patient group (15.1) was substantially higher than that for the parent group (11.2), 45% of the former having scores of 16 or greater compared with 24% of the latter. However, the overall pattern was generally similar in the two groups, with dysfunction most frequent in the domains of marriage and friendships and least frequent in work, negotiations, and everday coping. Similarly, men tended to have higher total scores than women (mean total of 13.7 and 11.9 with 43% and 23% respectively having total of scores of 16 or greater). The only appreciable sex difference in pattern was that women were marginally more likely to show dysfunction in love relationships, whereas they were less likely to show dysfunction in all other domains.

Measurement of general social dysfunction

In order to determine the extent to which dysfunction in each social domain (defined as a subscore of 3 or greater) reflected general social dysfunction (defined as a total score of 16 or greater), sensitivity and specificity coefficients were calculated for each social domain (Table III). There were substantial differences between domains in the pattern shown. Thus, non-intimate social contacts had both high sensitivity (0.87) and specificity (0.88); love relationships had high sensitivity (0.94) but only moderate specificity (0.62); whereas everyday coping had moderate sensitivity (0.67) but very high specificity (0.95).

TABLE III

Sensitivities and specificities of specific social domain dysfunctions as indicators of general social dysfunction (n = 97)

	Whole sample	*Parents*	*Patients*	*Men*	*Women*
Work					
Sensitivity	0.75	0.54	0.89	0.71	0.82
Specificity	0.92	0.95	0.87	0.93	0.92
Love relationships					
Sensitivity	0.94	0.92	0.95	0.90	1.00
Specificity	0.62	0.64	0.57	0.71	0.54
Friends					
Sensitivity	0.88	0.92	0.84	0.81	1.00
Specificity	0.74	0.76	0.70	0.71	0.76
Non-intimate social contacts					
Sensitivity	0.87	1.00	0.79	0.95	0.73
Specificity	0.88	0.90	0.83	0.82	0.92
Negotiations					
Sensitivity	0.63	0.77	0.53	0.62	0.64
Specificity	0.89	0.86	0.96	0.89	0.89
Everyday coping					
Sensitivity	0.63	0.46	0.74	0.57	0.73
Specificity	0.95	0.95	0.96	0.89	1.00

TABLE IV

Associations between dysfunction in specific social domains[1] *and general social dysfunction* (n = 97)

		Whole sample		Men		Women	
		Absent	*Present*	*Absent*	*Present*	*Absent*	*Present*
(a) Dysfunction in love relationships							
Total APFA score	<16	40	25	20	8	20	17
	16+	2	30	2	19	0	11
Sensitivity			0.94		0.90		1.00
Specificity			0.62		0.71		0.54
(b) Dysfunction in everyday coping							
Total APFA score	<16	62	3	25	3	37	0
	16+	12	20	9	12	3	8
Sensitivity			0.63		0.57		0.73
Specificity			0.95		0.89		1.00
(c) Dysfunction in non-intimate social contacts							
Total APFA score	<16	57	8	23	5	34	3
	16+	4	28	1	20	3	8
Sensitivity			0.87		0.95		0.73
Specificity			0.88		0.82		0.92

1. Dysfunction in specific social domain defined as score of 3 or more.

The meaning of these differences is easily appreciated through examination of the cross-tabulations, as shown in Table IV. The high specificity and sensitivity shown by non-intimate social contacts means that nearly all subjects with total APFA scores of 16 or greater showed dysfunction in this domain (28/32), whereas few of those with APFA scores of 15 or less did so (8/65). In other words, the score for this domain was a good indicator of general social dysfunction. Subjects with high APFA scores nearly always showed major problems in love relationships (30/32), but love relationship problems also occurred quite commonly in the absence of general social dysfunction (25/65). Conversely, difficulties in everyday coping rarely appeared as an isolated problem (3/65 subjects had APFA scores of 15 or less). When there was dysfunction in this domain, it was highly likely that there would be general social dysfunction (20/23 subjects) but over a third (12/32) of subjects with APFA scores of 16 or greater did not show dysfunction in everyday coping.

On the whole, these patterns applied similarly to patients and parents and to men and women but there were a few differences in emphasis. Thus, love relationship problems were particularly likely to appear as an isolated dysfunction in women; they did so in three-fifths of subjects (61%) compared with only 30% of men.

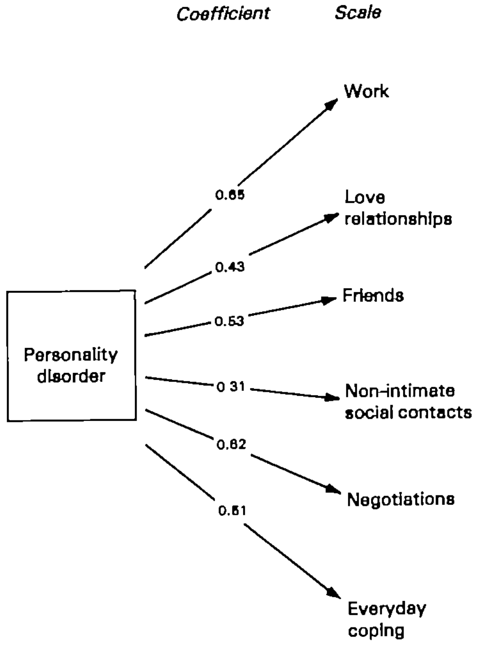

FIG. 3 Estimated measurement model for personality disorder (whole samples $n = 97$).

LISREL model of personality disorder

The data were also examined to estimate a measurement model for general social dysfunction. The model assumed that the scores from each social domain constituted continuous measures of a single latent variable, namely a hypothetical general social dysfunction factor, but that each score would be subject to 'error' in its reflection of this latent variable. In this connection, 'error' might arise either because the scores also reflected some other latent variable, such as qualities of functioning that were specific to that social domain, or because of measurement bias or unreliability. To achieve a satisfactory fit some correlation among these 'errors' had to be allowed. The eventual chosen model (goodness of fit $\chi^2 = 6.91$ with 6 d.f.) for the whole

TABLE V

LISREL latent variable coefficients for each social domain

Social domain	*Whole sample*	*Parents*	*Patients*	*Men*	*Women*
Work	0.65	0.51	0.66	0.64	0.68
Love relationships	0.43	0.35	0.46	0.57	0.32
Friends	0.53	0.55	0.55	0.45	0.55
Non-intimate social	0.62	0.65	0.55	0.65	0.50
Negotiations	0.30	0.39	0.24	0.45	0.24
Everyday coping	0.51	0.28	0.60	0.41	0.70

sample is shown in Fig. 3. The coefficients, which measure the degree to which the scale assesses only the latent general social dysfunction variable, confirm the picture obtained from study of sensitivities and specificities. Thus, the coefficients are highest for scores, such as work and non-intimate social contacts, with both high sensitivity and specificity (see Table V). Furthermore, the coefficients for groups disaggregated by sex and by patient/parent status confirmed that the quality of love relationships provided a less good reflection of general social dysfunction in women than in men (0.32 v. 0.57), and that coping assessed general social dysfunction less well in the parents of child-patients than in adults who had themselves been treated for psychiatric disorder (0.28 v. 0.61).

Similarly, although all the scales were intercorrelated through the latent general social dysfunction variable (which accounted for 55% of the variance), there were additional correlations between certain of them, as indicated in Table VI by the estimated correlations between the 'errors'. These correlated 'errors' could represent either artefacts of the rating process or associations across areas in actual functioning. The finding that the residual correlations were markedly different in each of the subgroups (see Table VI) suggests that measurement artefacts are unlikely to constitute the main explanation.

TABLE VI

LISREL analysis: residual correlations between social domains required for a latent variable model of personality disorder

Social domains	*Whole*	*Residual correlations*			
	sample	*Parents*	*Patients*	*Men*	*Women*
Work					
Love relationships	−0.32	−0.48	−0.18	−0.52	−0.08
Friends					
Non-intimate social contacts	0.25	0.05	0.40	0.10	0.13
Negotiations	0.26	0.30	0.26	0.25	−0.05
Everyday coping					

Rather it is probable that the correlations between 'errors' reflect true associations in pattern of social functioning.

Discussion

Our findings clearly indicate that people's social role performance in a range of social domains can be reliably rated using APFA. The intraclass correlation between raters of 0.87 for the total APFA score showed very high reliability and that for individual subscales was also good, with correlations in the 0.80s for three of the six domains and with only one correlation below 0.69 and none below 0.60. The spread of scores was also most satisfactory, with some individuals showing major problems in only one social domain and others doing so in all or almost all domains. The instrument demonstrably works well as a means of measuring the extent of social dysfunction and of identifying different patterns of dysfunction.

The results also show that it is appropriate to regard the total APFA score as a reflection of the degree of general social dysfunction. All the subscales were found to assess the hypothesised construct, or latent variable, of general dysfunction, although they differed in the extent and manner in which they did so. Some, such as 'everyday coping' were highly specific in this connection, so that it was rare for there to be general dysfunction without that domain being affected, but only moderately sensitive so that general dysfunction could be present with only limited dysfunction in that domain. Others, such as 'love relationships', showed the reverse pattern, meaning that specific dysfunction in that domain quite often occurred as an isolated problem but, on the other hand, when there was general social dysfunction it almost always involved impaired love relationships. In principle, it would be possible to create a scoring system for general dysfunction that took account of these differences between domains. However, weightings are notoriously unstable as a result of variations in pattern between different samples. That this would be likely to occur is evident in the finding that, to a minor extent, sensitivities and specificities varied according to patient/parent status and according to sex. Our findings suggest that further consideration of these and other differences (such as age) is warranted. Further empirical work will be necessary to determine how generalisable is the pattern found here. Nevertheless, it would be premature on the basis of this one, relatively small, sample to estimate, and then recommend, the use of particular subjects to group-specific weights or other equivalent changes to the rating procedure.

The LISREL modelling brought out another feature; namely that the single latent variable model fitted the data only if a negative residual correlation between the love relationship and friendship scales, and positive residual correlations between non-intimate social contacts and negotiations, and between negotiations and coping, were included. There could be several alternative explanations for these correlations. For example, the need for a negative residual correlation between love relationships and friendship could mean that when there are serious lasting difficulties in love relationships (usually marital discord in the groups studied) occurring as an isolated problem, the individuals tend to seek compensation in friendships. Conversely, those people who have a rewarding committed marital relationship may be less likely to seek extensive extrafamilial friendships. A greater negative correlation was needed in the parents' subgroup than with patients/ex-patients. This could mean that this pattern is most strongly established in older people (as parents tended to be older than patients) or that it is most applicable in individuals who do not suffer from psychiatric disorder. Again, further research is needed to explore these patterns and to determine the mechanisms involved. What is apparent from both the specificity and sensitivity data, as well as from the LISREL modelling, is that there are both specific and general social dysfunctions, and that further study of the associations between the two is needed.

In the meantime, it is reasonable to treat the total APFA score as a fair measure of general social dysfunction. The potential methodological problems stemming from complex, and varying, patterns of associations between subscales are less applicable when total APFA scores are high and when, therefore, by definition there is dysfunction in a majority of the social domains. It is for this reason, as well as others, that there is value in treating high scores, for example, scores of 16 or greater as used in our analyses,* as a categorical indicator of general social dysfunction. It is important, however, to appreciate that this is a matter of practical utility and not of a qualitative distinction. There are numerous hazards in inferring categories or dimensions from distributions (Grayson, 1987). There are many variables that can be regarded as *both* categorical and dimensional, the choice between approaches being based on the purposes for which the measure is being used. Thus, IQ demonstrably functions as a dimensional variable but, equally, severe mental handicap (defined in terms of an IQ below 50) is qualitatively distinct from normal IQ with respect to features such as life expectancy, fecundity and the role of single major gene effects (Rutter & Gould, 1985). But, within the below IQ 50 range, IQ still functions as a dimension for many purposes. The same may well apply to general social dysfunction. Regardless of whether such dysfunction involves qualitative distinctions from normality, it is likely that it may still be present in varying degrees. The present state of affairs is that whereas one may reasonably infer general social dysfunction from high total APFA scores, scores in the intermediate or lower range may reflect lesser degrees of the same variable or, alternatively, higher levels of specific dysfunction. Some guidance is provided by the pattern of APFA scores; thus the former is more likely when there is an even pattern of moderate dysfunction across domains and the latter when the same score is made up of a high score on one or two scales combined with low scores on others. However, the already noted need to take account of the varying pattern of association between subscales means that it is not yet possible to provide a mathematical expression for this differentiation.

The validity of the construct of general social dysfunction may be tested in several different ways. Previous research that has used a concept of personality disorder based on pervasive social dysfunction (but not using APFA as a measure) has shown it to have substantial temporal stability and predictive power (Rutter, 1977; Rutter & Quinton, 1984*a*, 1984*b*; Zeitlin, 1986). The findings suggest that the construct may have validity but it is necessary now to test it more directly using APFA. Such investigations are currently underway with the tests including temporal stability, correlations with childhood behaviour as measured previously in longitudinal studies, correlations with indicators of family psychopathology as studied at an earlier age, family genetic associations, and patterns of concordance in monozygotic and dizygotic twin pairs.

There is also the further question of whether general social dysfunction should be regarded as synonymous with the concept of personality disorder. For obvious reasons, psychiatrists are wary of diagnosing a psychiatric condition merely on the basis of social malfunction. Lewis (1953) clearly pointed out the dangers in doing so. If social malfunction is used as the basis for psychiatric diagnosis, it is not then possible to argue that a psychiatric condition is the cause of the social failure – that would be a meaningless tautology. It is for these, and similar, reasons that there have been numerous attempts to define personality disorder on the basis of specific psychological dysfunctions such as impulsivity, affective lability, self-destructive behaviour, lack of empathy, sensation-seeking, and lack of remorse (Siever & Klar, 1986). It may well be that the diagnosis of personality disorder should require the presence of such psychological dysfunction as well as impaired social role performance, but it is evident that the use of particular patterns of psychological dysfunction to define supposedly specific types of personality disorder does not work particularly well in practice (Rutter, 1987*a*; Siever & Klar, 1986). The problem is that mixed patterns are the rule rather than the exception. Moreover, both longitudinal and retrospective data suggest that there may be greater coherence in the construct of general social dysfunction than in particular varieties of personality disorder. Thus, conduct disturbance in childhood leads to both antisocial and non-antisocial, somatising and non-somatising varieties of personality disorder in adult life (Quinton *et al*, 1989; Robins, 1986; Zoccolillo *et al*, 1989; Zeitlin, 1986). Similarly, an institutional upbringing does the same (Quinton & Rutter, 1988; Rutter *et al*, 1989). It appears that what are needed are systematic studies to examine empirical associations between psychological traits or symptoms and general social dysfunction. For this purpose, we have undertaken a comparison between APFA scores and findings from a modified version of SADS–L (Harrington *et al*, 1988) as well as the Tyrer Personality Assessment Schedule (Tyrer *et al*, 1979; 1984); the results of that study will be reported separately.

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*As shown by our findings, a cut-off of 16 or greater works reasonably well as a way of selecting individuals with generalised social malfunction. Nevertheless, it is not claimed that this will ultimately prove to be the optimal cut-off point. Further work is necessary to test alternative cut-offs.

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References

American Psychiatric Association (1980) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn) (DSM-III). Washington DC: APA.

Bartko, J. J. & Carpenter, W. T. (1976) On the methods and theory of reliability. *Journal of Nervous and Mental Disease*, **163**, 307–317.

Breslau, N. (1987) Inquiring about the bizarre: false positives in diagnostic interview schedule for children (DISC): ascertainment of obsessions, compulsions and psychotic symptoms. *Journal of the American Academy of Child Psychology*, **26**, 639–644.

Brown, G. W. & Rutter, M. L. (1966) The measurement of family activities and relationships: a methodological study. *Human Relations*, **19**, 241–263.

Clarkin, J., Widiger, T., Frances, A. J., *et al* (1983) Prototypic typology and the borderline personality disorder. *Journal of Abnormal Psychology*, **92**, 263–275

Cohen, J. (1968) Weighted kappa: nominal scale agreement with provision for scaled disagreement of partial credit. *Psychological Bulletin*, **70**, 213–230.

Docherty, J. P., Fiester, S. J. & Shea, T. (1986) Syndrome diagnosis and personality disorder. In *American Psychiatric Association Annual Review*, Vol. 5 (eds A. J. Frances & R. E. Hales). Washington DC: American Psychiatric Association.

Frances, A. J. & Widiger, T. (1986) The classification of personality disorders: an overview of problems and solutions. In *American Pyschiatric Association Annual Review*, Vol. 5 (eds A. J. Frances & R. E. Hales). Washington DC: American Psychiatric Association.

Graham, P. & Rutter, M. (1968) The reliability and validity of the psychiatric assessment of the child. II. Interview with the parent. *British Journal of Psychiatry*, **114**, 581–592.

Grayson, D. A. (1987) Can categorical and dimensional views of psychiatric illness be distinguished? *British Journal of Psychiatry*, **151**, 355–361.

Harrington, R., Hill, J., Rutter, M., *et al* (1988) The assessment of lifetime psychopathology: a comparison of two interviewing styles. *Psychological Medicine*, **18**, 487–493.

John, K. & Weissman, M. M. (1987) The measurement of psychosocial and familial aspects of depression. In *The Measurement of Depression: Clinical, Biological, Psychological and Psychosocial Perspectives* (eds A. J. Marsella, R. M. A. Hirschfeld & M. Ratz), pp. 344–375. New York: Guilford Press.

Joreskog, K. G. & Sorbum, D. (1981) LISREL V: Analysis of linear structural relationships by maximum likelihood and least squares methods. *Research Report 81–88*. University of Uppsala.

Katschnig, H. (1983) Methods for measuring social adjustment. In *Methodology in Evaluation of Psychiatric Treatment* (ed. T. Helgason), pp. 205–218. New York: Cambridge University Press.

Le Couteur, M., Rutter, M., Lord, C., *et al* (1989) Autism diagnostic interview: a standardized investigator-based instrument. *Journal of Autism and Developmental Disorders* (in press).

Lewis, A. J. (1953) Health as a social concept. *British Journal of Sociology*, **4**, 109–124.

Mann, A. H., Jenkins, R., Cutting, J. C., *et al* (1981) The development and use of a standardized assessment of abnormal personality. *Psychological Medicine*, **11**, 839–847.

Mellsop, G., Varghese, F., Joshua, S., *et al* (1982) The reliability of axis 2 of DSM-III. *American Journal of Psychiatry*, **139**, 1360–1361.

Merikangas, K. & Weissman, M. M. (1986) Epidemiology of DSM-III Axis II: personality disorders. In *American Psychiatric Association Annual Review*, Vol. 5. (eds A. J. Frances & R. E. Hales), pp. 258–278. Washington DC: American Psychiatric Association.

Quinton, D. & Rutter, M. (1988) *Parenting Breakdown: The Making or Breaking of Intergenerational Links*. Aldershot: Gower Publishing.

——, —— & Gulliver, L. (1989) The social functioning in early adulthood of the children of psychiatric patients. In *Straight and Devious Pathways From Childhood to Adulthood* (eds L. N. Robins & M. Rutter). New York: Cambridge University Press (in press).

Reich, J. (1985) Measurement of DSM-III, Axis II. *Comprehensive Psychiatry*, **26**, 352–363.

Robins, L. N. (1966) *Deviant Children Grown Up*. Baltimore: Williams and Wilkins.

—— (1978) Sturdy childhood predictors of adult antisocial behaviour: replications from longitudinal studies. *Psychological Medicine*, **8**, 611–622.

—— (1986) The consequences of conduct disorder in girls. In *Development of Antisocial and Prosocial Behavior: Research, Theories and Issues* (eds D. Olweus, J. Block & M. Radke-Yarrow), pp. 385–414. New York: Academic Press.

Rutter, M. (1966) *Children of Sick Parents: An Environmental and Psychiatric Study*. Institute of Psychiatry Maudsley Monograph No 16. London: Oxford University Press.

—— (1977) Prospective studies to investigate behavioural change. In *The Origins and Course of Psychopathology* (eds J. S. Strauss, H. M. Babigian & M. Roff), pp. 223–247. New York: Plenum Publishing.

—— (1984) Psychopathology and development. I. Childhood antecedents of adult psychiatric disorder. *Australian and New Zealand Journal of Psychiatry*, **18**, 225–234.

—— (1987*a*) Temperament personality and personality disorder. *British Journal of Psychiatry*, **150**, 443–458.

—— (1987*b*) Parental mental disorder as a psychiatric risk factor. In *American Psychiatric Association Annual Review*, Vol. 6 (eds R. E. Hales & A. J. Frances). Washington DC: American Psychiatric Association.

—— & Brown, G. W. (1966) The reliability and validity of measures of family life and relationships in families containing a psychiatric patient. *Social Psychiatry*, **1**, 38–53.

—— & Quinton, D. (1984*a*) Parental psychiatric disorder: Effect on children. *Psychological Medicine*, **14**, 853–880.

—— & —— (1984*b*) Long-term follow-up of women institutionalized in childhood: factors promoting good functioning in adult life. *British Journal of Developmental Psychology*, **2**, 191–204.

—— & Gould, M. (1985) Classification. In *Child and Adolescent Psychiatry: Modern Approaches* (2nd edn) (eds M. Rutter & L. Hersov) pp. 304–321. Oxford: Blackwell Scientific.

—— & Pickles, A. (1989) Improving the quality of psychiatric data: classification, cause and course. In *Methodological Issues in Longitudinal Research I: Data and General Designs* (ed D. Magnusson). Cambridge: Cambridge University Press (in press).

——, Quinton, D. & Hill, J. (1989) The effects of an institutional rearing on social functioning in early adult life in men and women. In *Straight and Devious Pathways from Childhood to Adulthood* (eds L. N. Robins and M. Rutter). Cambridge: Cambridge University Press (in press).

Siever, L. J. & Klar, H. (1986) A review of DSM-III criteria for the personality disorders. In *American Psychiatric Association Annual Review*, Vol. 5 (eds A. J. Frances & R. E. Hales), pp. 279–314. Washington DC: American Psychiatric Association.

Stangl, D., Pfohl, B., Zimmerman, M., *et al* (1985) A structured interview for the DSM-III personality disorders: a preliminary report. *Archives of General Psychiatry*, **42**, 591–596.

Sturt, E. & Wykes, T. (1987) Assessment schedules for chronic psychiatric patients. *Psychological Medicine*, **17**, 485–494.

Tarnopolsky, A. & Berelowitz, M. (1987) Borderline personality: a review of recent research. *British Journal of Psychiatry*, **151**, 724–734.

Tyrer, P. & Ferguson, B. (1987) Problems in the classification of personality disorder. *Psychological Medicine*, **17**, 15–20.

——, Alexander, M. S., Cicchetti, D., *et al* (1979) Reliability of a schedule for rating personality disorder. *British Journal of Psychiatry*, **135**, 168–174.

——, Cicchetti, D. V., Casey, R. R., *et al* (1984) Cross-national reliability study of a schedule for assessing personality disorders. *Journal of Nervous and Mental Disease*, **172**, 718–721.

Weissman, M. M. (1975) The assessment of social adjustment: a review of techniques. *Archives of General Psychiatry*, **32**, 357–365.

——, Sholomskas, D. & John, K. (1981) The assessment of social adjustment: an update. *Archives of General Psychiatry*, **38**, 1250–1258.

World Health Organization (1978) *International Classification of Diseases* (9th revision). Geneva: WHO.

Zeitlin, H. (1986) *The Natural History of Disorder in Childhood*. Institute of Psychiatry Maudsley Monograph No 29. London: Oxford University Press.

Zoccolillo, M., Rutter, M., Quinton, D., *et al* (1989) The outcome of conduct disorder: implications for defining adult personality disorders (in preparation).

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Psychiatric Symptoms, Cognitive Stress and Vulnerability Factors
A Study in a Remand Prison

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In a consecutive sample of 208 male prisoners interviewed on the tenth day (T1) after entry, high levels of psychiatric symptoms as measured by the GHQ were recorded. These GHQ scores were strongly correlated with perceived worries and concerns of the prisoners ('cognitive stress'). After 60 days of detention (T2), a significant fall in GHQ scores was observed, and they were still correlated with cognitive stress. A significant *negative* correlation between cognitive stress at T1 and GHQ scores at T2 was observed. The relationship between potential vulnerability factors (life experiences, social network, personality factors) and GHQ scores was not strong at either T1 or T2. Psychiatric symptoms are common during the early phase of imprisonment but are not durable.

A remand prison constitutes an environment with high levels of stress, resulting from abrupt changes in social support networks and uncertainty about the future. Our experience in the medical service of the Geneva remand prison shows that various forms of reactive states with both anxiety and depressive symptoms are common in prisoners, but are frequently of short duration and rarely take the form of a depressive illness (Harding, 1984). In a series of 53 suicide attempts at the prison, depressive illness was noted in only ten cases (Guignet, 1981).

In a research project on the effect of early stages of imprisonment on mental health, we have already described the high level of consultations and recourse to psychotropic medication in the early weeks of stay in the Geneva remand prison (Zimmermann & von Allmen, 1985). However, Mechanic (1978) would not accept that help-seeking is necessarily a good indicator of morbidity.

In this paper, we examine the relationship between vulnerability factors, cognitive stress, and psychiatric symptoms during the early weeks of imprisonment. Vulnerability factors were considered as a combination of early life events, recent social status, and abnormal personality traits, which might adversely affect the individual's capacity to cope with stress on entry to prison. Cognitive stress includes worries and concerns about the current situation, without necessarily associated unpleasant feelings of dysphoria or anxiety. The data come from two systematic, structured interviews carried out 10 (T1) and 60 days (T2) after entry into a remand prison, in a consecutive series of male prisoners.

Our aim was to identify the possible effect of a series of potential vulnerability factors on both cognitive stress and psychiatric symptoms, to test whether cognitive stress could be distinguished from psychiatric symptoms, and to examine the relationship between cognitive stress and symptoms. The conceptual model of the research design is represented in Fig. 1.

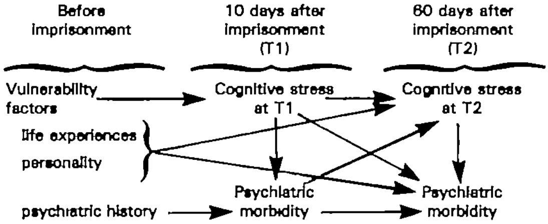

FIG. 1. Conceptual model of the research design. The arrows indicate the relationships examined in the analysis of results.

Method

Personal interviews were conducted by trained research workers with 208 remand prisoners at the Geneva prison at T1. Informed consent was obtained in the following way. Prisoners received a note from the director of the prison, inviting them to take part in a research interview designed to investigate the way people react to imprisonment, but assuring them that they were free to refuse. The research procedure was explained by the research worker before the structured interview. The interview was not carried out in the medical service. There were only three refusals. A further two cases were excluded because of language difficulties. Thus 208 subjects (98%) out of a consecutive series of 213 were included. Women prisoners were excluded from the study. Of these 208 prisoners, 91 were still present and were reinterviewed at T2 (which for practical reasons fell between the 58th and 62nd day). Due to the international character of the prison, personal interviews were conducted in four languages (French, German, English, and Spanish).

Data were collected using a number of standardised research instruments.

Psychiatric symptoms

In order to measure psychiatric symptoms, we used Goldberg's (1978) 28-item General Health Questionnaire (GHQ) at both T1 and T2. The GHQ was not used as the first stage of a two-stage case-detection procedure, but rather as a measure of psychiatric symptoms at two points in time. Developments in scoring techniques for the GHQ allow an estimation not only of overall psychiatric symptoms, but also of anxiety, depression, psychosomatic symptoms, and social dysfunction.

Cognitive stress

In order to evaluate cognitive stress, we asked the following question: "In your present situation, what are the things you are most worried about?". The aim was to identify the perceived level of worries and concerns. Based on responses to a pilot study, a check list of 24 items was presented, relating to three distinct areas:

(a) the subject's personal relationships
(b) the subject's professional and economic situation
(c) the offence, the criminal procedure, and the likely sentence.

For each item, the subject could tick one of five possible answers: extremely, very much, quite, a little, not at all. Unlike the GHQ items referring to the ways the subject feels about himself, cognitive stress items were meant to measure the subject's worries about elements of the social environment.

All these items were then combined in a reliable summative scale for T1 ($\alpha = 0.89$) and T2 ($\alpha = 0.90$). This scale measures for each subject a subjective state, which we call 'cognitive stress'. A common-factor analysis of this measure yielded the following seven factors (66% explained variance at T1 and 72% at T2):

(a) worries about the welfare of family members and of others in significant, close relationships (father, mother, brothers, and sisters)
(b) worries about being rejected by the family and others in significant, close relationships
(c) feelings of shame and guilt regarding offences
(d) worries about the judge's hostility and lack of understanding
(e) worries about professional and personal future
(f) worries about length of remand and fear of a severe sentence
(g) worries about being rejected by fellow prisoners and prison guards.

Vulnerability factors

Three kinds of vulnerability factors are considered.

(a) Life experiences

Unhappy childhood, early separation from parents, and more generally the experience of numerous negative life events were measured by a series of structured interview questions. With regard to current life situation, we took into account educational level, employment over the 12 months preceding incarceration, and a measure of recidivism. Finally, we investigated the subject's personal relationships in terms of (i) the presence or absence of a significant relationship (wife, steady girlfriend), and (ii) overall frequency of social contacts.

(b) Personality

Pathology of the personality has been evaluated on the basis of the Minnesota Multiphasic Personality Inventory (MMPI, in a short form called Minimult) (Hathaway & McKinley, 1981). Each subject's profile was established and then inspected by an experienced clinical psychologist. Each subject was classified into one of four categories: (i) 'normal'; (ii) 'neurotic traits without character disorder', (iii) 'neurotic traits with character disorder'; and (iv) 'severe personality disorders'. Levels of self-esteem were measured by four standard questionnaire items related to feelings about self worth.

(c) Medical history

Self-reported medical history data are limited to the presence of prior psychiatric problems, regular use of hypnotic and tranquillising medication, and drug and alcohol abuse.

Results

The results are presented in a sequential manner, with psychiatric symptoms (GHQ scores) as the unifying theme. After describing the sample, we examine the evolution of GHQ scores between T1 and T2. There follows an analysis of the differentiation and associations between cognitive stress and psychiatric symptoms at T1 and T2. Finally, we examine the associations between various vulnerability factors and symptoms.

The sample

About half of the sample were aged between 18 and 29 years; a minority were married. Fifty per cent had received no more than primary school education, and most held unskilled and unstable jobs, if any. Only about a third of interviewed subjects had been regularly employed during the year preceding imprisonment. More than half of the subjects had already been in prison. Offences were predominantly theft, house-breaking, or drug-related. Serious violent offences were reasons for imprisonment in about 15% of the cases. A third of the subjects were considered as socially well integrated before imprisonment on the basis of our initial interviews (i.e. stable work and social relationships).

The MMPI personality tests indicated that a third of the subjects were within the normal range regarding personality traits, 38% showed neurotic traits and/or character disorders, and 29% suffered from rather severe personality disorders (instability, impulsivity, low tolerance of frustration). As expected, lack of social integration and psychological impairment were strongly associated.

A minority of the subjects (25%) mentioned that they were not satisfied with their general health before imprisonment, while 35% estimated that they had problems

TABLE I
GHQ scores at T1 ($n_1=200$)

GHQ scales	*Mean*	*Median*	*95% confidence intervals*	*% high scoring subjects*	*Reliability (α)*
Somatic symptoms	3.4	3.5	(3.1– 3.7)	50	0.76
Anxiety and insomnia	4.3	4.9	(4.0– 4.7)	64	0.82
Social dysfunction	3.5	3.4	(3.2– 3.8)	48	0.76
Depression	2.5	2.1	(2.2– 2.9)	30	0.84
Total severity	13.8	14.4	(12.8–14.8)	57	0.90

1. GHQ28 '0-0-1-1' scoring method for % high-scoring subjects: scores >3.0, except for total severity, where scores >12.0.

regarding their psychological health, with 17% reporting at least one suicide attempt.

Present or past drug dependence (heroine, cocaine, morphine) was reported by 34% of the subjects; self-reported drinking habits indicated that 15% of the subjects had an alcohol-related problem. About a third of the sample were taking tranquillisers and/or hypnotics regularly during the three months before imprisonment.

GHQ symptom reports at T1

Adopting relatively high threshold scores, 57% of the subjects manifested high levels of psychiatric symptoms at T1 (Table I).

More than half of the subjects would therefore be considered as potential psychiatric cases, justifying a follow-up psychiatric diagnostic interview. For ethical and practical reasons, we were unable to conduct such in-depth investigations. Clinical experience at the Champ-Dollon medical service, however, indicates that serious depressive illness is rare in the prison population (Harding, 1984). We believe that the majority of high-scoring subjects suffer from reactive states that are often self-limiting in nature. The prison's medical service deals with such 'reactive states', typically with weekly consultations, and prescriptions of hypnotics and tranquillisers. Psychiatrists deal with about 10% of the total case load.

The high correlations of the four subscales with the total GHQ scale, shown in Table II, may indicate that global distress is reflected, as we would expect, in the reporting of relatively undifferentiated psychiatric symptoms. Moreover, total GHQ scores are most highly correlated with the scores on the anxiety subscales, which tends to substantiate that stress-induced psychic tension is the underlying phenomenon.

GHQ – change or stability

In comparing results between T1 and T2, we have considered scores at T1 only for those subjects who were still in prison at T2 (Table III).

Over the two-month period we observed a drop of the mean severity score in all GHQ scales. Drops are statistically significant ($P<0.05$) except for the depression scale. Decline of symptoms is most marked on 'social dysfunction'. An inspection of the individual scale items shows that psychosomatic symptoms decline most (e.g. headaches, cold spells, feeling sick, sleep disturbance), along with being able to keep busy and find some pleasure in various daily activities. The global level of psychiatric symptoms is quite strongly correlated over time ($r_{T1-T2}=0.61$).

Two explanations may be put forward.

(a) The decline of symptoms from T1 to T2 is not real. Subjects apply a different threshold to the standard 'more', 'less', and 'as usual' possible answers at T1 and T2, simply as a consequence of the 'chronicity' of the psychological distress – they grow to accept their psychological suffering as 'normal'. Furthermore, it is likely that the number of positive responses as an equivalent of help-seeking behaviour diminishes. By T2 the various sources of support are already mobilised, and some form of medical care is often underway.

(b) There is a real change. Symptoms decrease because subjects adapt to detention, the novelty of the stressful experience diminishes, and various forms of coping reduce psychological stress; consequently symptoms associated with such stress diminish.

There is no way of assessing the relative importance of each explanation, but it is likely that both contribute.

TABLE II
Intercorrelations between the four scales and the total GHQ scores at T1 (n=200) and T2 (n=88)

	Anxiety and insomnia		*Social dysfunction*		*Depression*		*Total GHQ score*	
	T1	*T2*	*T1*	*T2*	*T1*	*T2*	*T1*	*T2*
Somatic symptoms	0.54	(0.54)	0.41	(0.42)	0.40	(0.54)	0.76	(0.74)
Anxiety and insomnia	–	–	0.53	(0.68)	0.45	(0.66)	0.82	(0.88)
Social dysfunction	–	–	–	–	0.42	(0.62)	0.76	(0.82)
Depression	–	–	–	–	–	–	0.75	(0.87)

TABLE III
GHQ scores at T1 and T2 (n = 88)

GHQ scales	*Mean*	*Median*	*95% confidence intervals*	*% high-scoring subjects*	*Reliability (α)*
Somatic symptoms					
T1	3.4	3.4	(3.0– 3.9)	49	0.68
T2	2.8	2.7	(2.3– 3.3)	40	0.77
Anxiety and insomnia					
T1	4.3	4.9	(3.8– 4.8)	64	0.83
T2	3.5	3.7	(2.9– 4.0)	52	0.87
Social dysfunction					
T1	3.6	3.5	(3.1– 4.0)	50	0.75
T2	2.6	2.2	(2.1– 3.0)	32	0.80
Depression					
T1	3.0	2.7	(2.4– 3.5)	39	0.87
T2	2.4	1.4	(1.9– 3.0)	30	0.87
Total severity					
T1	14.3	15.3	(12.8–15.7)	62	0.89
T2	11.3	9.7	(9.6–13.0)	43	0.93

GHQ28 '0-0-1-1' scoring method for % high-scoring subjects: scores >3.0, except for total severity, where scores >12.0.

Cognitive stress and GHQ symptoms

Correlations between indices of cognitive stress and the total GHQ scores (at T1 and T2) are statistically significant ($P<0.001$) and moderately high ($r_{T1}=0.46$; $r_{T2}=0.59$). This finding confirms the hypothesis about a positive relationship between subjective stress (existential worries) and reporting of psychiatric symptoms. But this finding also indicates that many subjects, although highly stressed, do not report psychiatric symptoms, and that others, although moderately stressed, report many symptoms.

At T1, the relationship between cognitive stress and individual symptoms is complex. Low levels of cognitive stress are generally protective in terms of symptoms, although 40% of low stressed subjects experienced sleeplessness. However, median levels of stress are more strongly associated with increased symptom levels than high levels, except in the case of anxiety (Fig. 2).

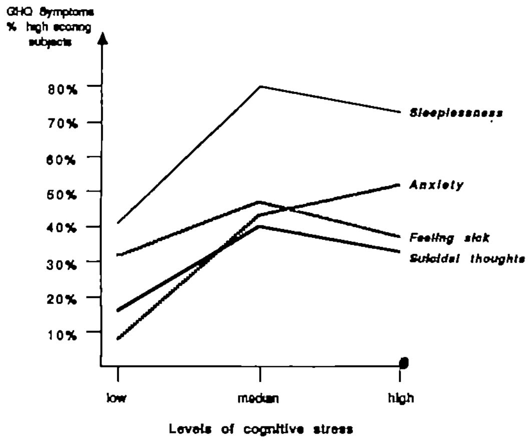

FIG. 2 Levels of cognitive stress and GHQ symptoms at T1.

At T2, the relationship is more straightforward. As expected, low cognitive stress is definitely protective, while high levels of stress elicit the highest symptom levels (Fig. 3).

These observations lend some support to the idea of different phases in stress-induced reactions. In the acute phase, symptom patterns appear paradoxical, in relation to perceived stress, while in the subacute phase the relationship is more direct.

We have examined the relationship between cognitive stress and psychiatric symptoms at T1 and T2 respectively by the statistical technique of path analysis (Asher, 1982). The results (Fig. 4) show a strong 'carry-over' effect, despite the fact that overall levels of stress and symptomatology both tend to decline between T1 and T2. Furthermore, psychiatric symptoms at T2 are strongly predicted by corresponding symptoms at T1 and cognitive stress at T2. This result confirms the strong impact of cognitive stress on symptoms independently of initial symptom levels: existential worries (cognitive stress) resulting from the stressful situation are to a very significant extent responsible for psychiatric symptoms.

However, we observe that subjects who experience high levels of cognitive stress at T1 tend to have lower overall distress symptomatology at T2: being aware of the stressful reality early in their prison experience appears to have a prophylactic effect with regard to the appearance of symptoms later in time; this is especially true for subjects whose cognitive stress is not already associated with psychiatric symptoms at T1.

Symptoms reported at T1 have no statistically significant impact on later levels of cognitive stress. This tends to confirm our hypothesis that it is possible to measure cognitive stress separately from psychiatric symptoms. It remains, however, certain that suffering caused by such

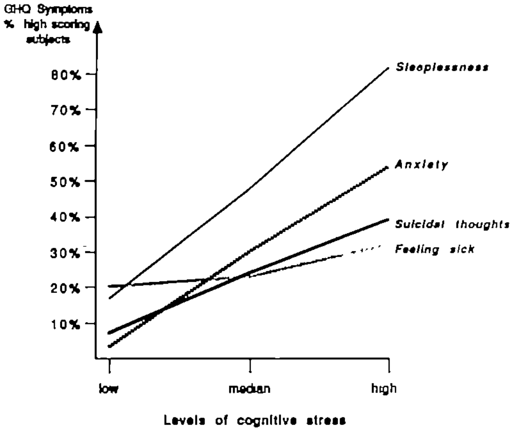

FIG. 3 Levels of cognitive stress and GHQ symptoms at T2.

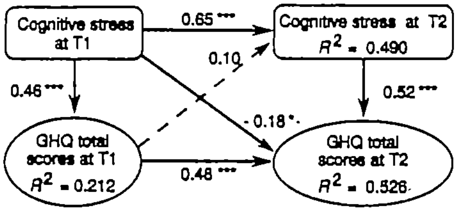

FIG. 4 Path analysis of cognitive stress and GHQ scores at T1 and T2 (path model results, $n = 91$). Significance levels of standardised β coefficients: $^{*}P<0.10$, $^{**}P<0.05$, $^{***}P<0.001$.

stress results to a significant extent in distress as expressed by symptom reports.

Although stress tends to produce symptoms, it appears on the basis of these findings that it is profitable to view the two as distinct, but related phenomena.

Personality disorder and psychiatric symptoms

The relationship between personality typology and average GHQ scores is shown in Fig. 5.

(a) Subjects without personality disorders (type A in Fig. 5) experience significantly lower levels of distress.
(b) Levels of anxiety are significantly higher for subjects presenting neurotic traits (types B and C).
(c) Depressive symptoms are particularly severe among the subjects combining neurotic traits and character disorders (type C). Profound feelings of dissatisfaction with themselves and a propensity for acting out making these subjects at high risk for suicide.
(d) Subjects suffering from severe personality disorders (instability, aggression, impulsiveness) (type D) experience a relatively low level of distress and come close to the normal subjects.

Regardless of the presence or not of personality disorders, symptom severity declines between T1 and T2. As one would expect, 'normals' (type A) change relatively little given their low initial level of symptoms. The drop in symptom severity is strongest among the subjects with neurotic traits only (type B).

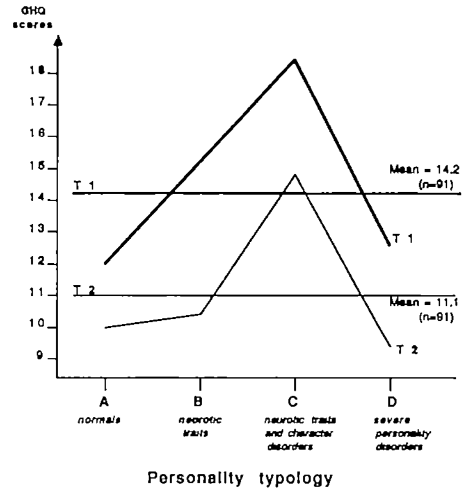

FIG. 5 Personality and GHQ scores

Selected vulnerability factors and cognitive stress

From the large array of data on personal and medical history and personality, we have selected certain variables which seem *a priori* likely to influence cognitive stress and/or psychiatric symptoms. Nine such factors are shown in Fig. 6. At T1, a number of these factors have no significant relationship with cognitive stress: frequency of social contacts, happy childhood, neurotic personality traits, character disorders, and prior mental health problems. The strongest predictor of stress is a significant female relationship. In other circumstances such a relationship is protective, but clearly, on entry to prison, the loss of a close, intimate personal contact has an immediate effect on perceived stress in the acute phase, while subjects without such privileged relationships are protected. Subjects with low self-esteem, with alcohol dependency or prior drug abuse are also protected from cognitive stress. The acute prison experience is perhaps not perceived as so negative in terms of their general life experience.

Selected vulnerability factors and GHQ symptoms

In Table IV, we present β coefficients between selected vulnerability factors and GHQ symptoms at both T1 and T2, with the intervening variable cognitive stress controlled for. In general, we are impressed by the lack of apparent effect of potential vulnerability factors, especially at T1. Acute-phase stress reactions appear to be largely dependent on the 'here and now' experience, leading to cognitive stress and subsequently symptoms, especially anxiety. It is noteworthy that factors such as 'happy childhood', character disorders, and prior mental health problems have

TABLE IV

Selected vulnerability factors related to GHQ symptom scales controlling for cognitive stress (regression analysis results)

Independent variables	*Somatic items*		*Anxiety items*		*Depression*		*Total GHQ severity*	
	T1	*T2*	*T1*	*T2*	*T1*	*T2*	*T1*	*T2*
Cognitive stress	0.21*	−0.01	0.36**	0.41**	0.21*	0.24**	0.35***	0.30**
Happy childhood	0.01	−0.06	−0.05	0.02	−0.16*	−0.04	−0.03	0.02
Significant female relationship	0.01	0.15*	0.19*	0.30**	0.09	0.26**	0.15	0.35***
Neurotic personality traits	0.04	0.38**	0.09	0.25**	0.33***	0.36***	0.27**	0.39***
Character disorders	−0.08	0.30	−0.13	0.02	0.15	0.16*	−0.01	0.17*
Self-esteem	−0.10	−0.06	−0.12	−0.01	−0.21*	−0.07	−0.17	−0.05
Prior mental health problems	0.16	0.08	−0.12	0.07	−0.03	0.12	0.02	0.05
Drug abuse	0.28**	0.03	0.14	0.04	−0.02	0.06	0.10	0.08
Variance explained: R^2	0.167	0.356	0.268	0.465	0.400	0.439	0.360	0.547
Variance explained (adjusted): $\bar{R}^2$	0.076	0.283	0.187	0.407	0.335	0.376	0.288	0.495
F value: F	1.8	4.9	3.3	7.9	6.1	7.0	4.9	10.6
Significance level: P	0.085	0.000	0.003	0.000	0.000	0.000	0.000	0.000
Number of cases: n	83	81	83	81	83	81	83	81

Note: Significance levels of standardised β coefficients: $^*P<0.10$, $^{**}P<0.05$, $^{***}P<0.001$.

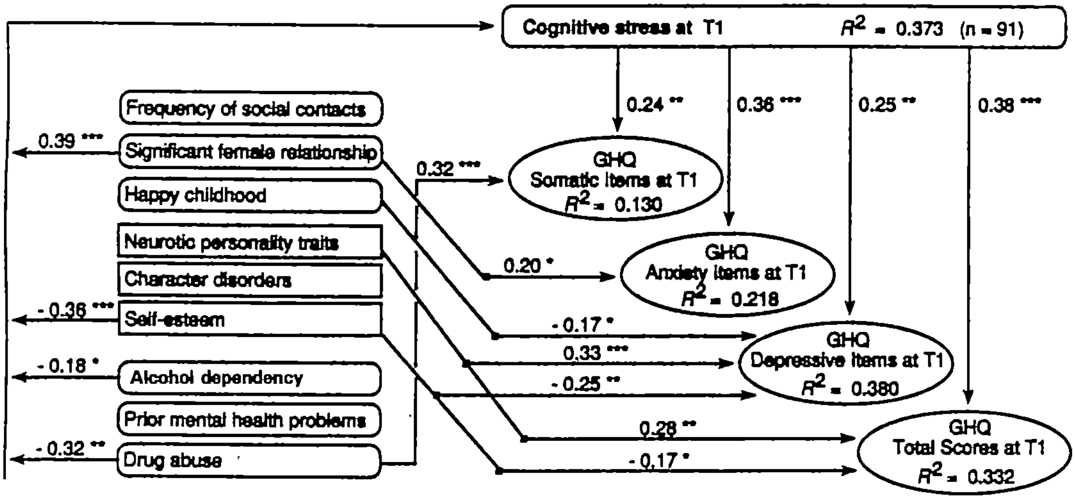
Cognitive stress at T1
R² = 0.373 (n = 91)
0.24 **
0.36 ***
0.25 **
0.38 ***
Frequency of social contacts
0.39 ***
Significant female relationship
Happy childhood
Neurotic personality traits
Character disorders
- 0.36 ***
Self-esteem
- 0.18 *
Alcohol dependency
Prior mental health problems
- 0.32 **
Drug abuse
0.32 ***
GHQ Somatic items at T1 R² = 0.130
0.20 *
GHQ Anxiety items at T1 R² = 0.218
- 0.17 *
0.33 ***
- 0.25 **
GHQ Depressive items at T1 R² = 0.380
0.28 **
- 0.17 *
GHQ Total Scores at T1 R² = 0.332

FIG. 6 Cognitive stress, vulnerability and GHQ symptoms at T1 – path-model results, showing standardised β coefficients ($n=91$). Significance levels of standardised β coefficients: $^*P<0.01$, $^{**}P<0.05$, $^{***}P<0.001$.

little or no measurable effect on the occurrence of symptoms. However, neurotic personality traits and a significant female relationship do appear as risk factors, more markedly at T2 than T1.

In Fig. 6, standardised coefficients are also presented between vulnerability factors and GHQ symptoms at T1. Several factors appear to influence symptoms, without influencing cognitive stress. Notably, neurotic personality traits are associated with high scores on depression and high total GHQ scores.

The path-model analyses confirm that cognitive stress and psychiatric symptoms can be statistically differentiated, and that vulnerability factors act independently on the two phenomena. The different nature of symptoms and of risk factors in the acute and subacute phases is also striking.

Discussion

If stressful life events are defined as any set of circumstances that requires changes in the basic life pattern of an individual (Holmes & Rahe, 1967), then imprisonment may be considered highly stressful. However, stressors such as separation from family and friends, loss of job, the promiscuity of prison life, and uncertainty about the future may have different meanings for individuals. The stress experience depends on the individual's cognitive appraisal and his perception of his own capacities to cope with the situation (Lazarus, 1981). For example, a married middle-aged man in a steady job entering prison for the first time would probably experience more stress than a homeless, unemployed man who knows prison well. Stress should not therefore be taken for granted, but measured. This we have attempted to do in this study.

There is cumulative hard epidemiological evidence that stressful life situations are associated with increased psychological disturbance and a greater probability of psychopathological behaviour (Thoits, 1982). Depressive symptoms are perhaps the most common manifestation of psychological distress:

> "vulnerability factors such as low self-esteem and social support, and also the severity of the stressor itself are likely to determine in most instances whether [distress] reaches the formal criteria of clinical depression." (Brown *et al*, 1985)

There is, however, considerable debate and disagreement as to what extent such reactive depression should be labelled 'disease' rather than 'distress' (Brown *et al*, 1985).

Our results suggest that entry into prison is a stressor, and that one can clearly distinguish cognitive stress, that is to say a perception of a state of existential worries and concerns from psychiatric symptoms, present in a high proportion of subjects and more so during the acute phase. Our results must however be placed in the context of previous observations on psychiatric disorders in prisoners, in view of the specificity of the prison experience, as illustrated by the increased risk for stress and symptoms in subjects with close female relationships before imprisonment. In normal circumstances such relationships would be protective.

Prisoners constitute a high-risk group for psychiatric disorders. The reasons have been succinctly stated by Gunn (1986):

> ". . . not only do prisons generate psychiatric problems but they also collect them inappropriately and act as unofficial mental hospitals for individuals who should be in health care. . .".

For the health professional working within the prison system, the two mechanisms of psychiatric pathogenesis among prisoners create serious ethical and clinical problems.

'Prison-generated' stress disorders, which can lead to seriously disabling states, self-mutilations, and suicide, are difficult to manage and even more difficult to prevent, since the origin of the stress is beyond the influence of the health professional. Stress is not only related to the prison environment (deprivation of liberty, overcrowding, promiscuity, conflicts and tensions among inmates, and between guards and inmates) but also to the legal process (court appearances, interrogation, contacts with lawyers), and to the rupture in the prisoner's previous social network.

Coid (1984) has reviewed 11 studies on the prevalence of mental disorders among prisoners: high rates of mental retardation, alcoholism, and personality disorders were the outstanding features. Gunn *et al* (1978) found high rates of anxiety and depression during the first phases of imprisonment, with a significant fall over the next six months. These conclusions are based on the results of questionnaires such as the GHQ. But what do such results mean within the prison setting? To feel sad and tense while in prison awaiting trial would seem to many people a 'normal' reaction. Is it unhealthy? Does the increased risk of suicidal acts indicate the 'tip of the iceberg' of a high prevalence of psychiatric morbidity? By measuring such phenomena, the researcher faces the same ethical dilemmas as the prison doctors who have to decide how to manage them. Whereas in normal medical practice, the health professional tries to modify stress factors within the environment, in prison the medical services are unable to do so, and have often little or no possibility of defining the stress factors operating on an individual. The result is that interventions are often ineffective and sometimes inappropriate, for example, the prescription of prolonged courses of benzodiazepines, leading to dependence.

Our results confirm the high rates of psychiatric symptoms among prisoners. They also show that symptoms, as well as levels of cognitive stress, tend to fall during the first two months of imprisonment. Coping mechanisms do seem to be available, at least to some prisoners. Zimmermann (1988) has shown that prisoners receive more support from other prisoners than they predict themselves at the tenth day. This implies that medical services within the prison should help prisoners to help themselves, rather than offering a blanket response to stress-induced symptoms by anxiolytic medication.

It would also seem important for medical staff to distinguish clearly between expressed worries and concerns ('cognitive stress') and psychiatric symptoms. Our finding that high levels of cognitive stress early in imprisonment are protective in terms of symptoms after two months would suggest that expressing concerns during the acute phase of stress should be encouraged, and that supportive interviews would be more appropriate than psychotropic medication when cognitive stress is not accompanied by clear psychiatric symptoms.

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References

ASHER, H. B. (1976) Causal modeling. In *Quantitative Application in the Social Science*: No. 3. Sage University Papers. Beverly Hills: Sage.

BROWN, G. W., CRAIG, T. K. J. & HARRIS, T. O. (1985) Depression: distress or disease? Some epidemiological considerations *British Journal of Psychiatry*, 147, 612–622.

COID, J. (1984) How may psychiatric patients in prison? *British Journal of Psychiatry*, 145, 78–86.

GOLDBERG, D. (1978) *Manual of the General Health Questionnaire*, Slough: National Foundation for Education Research.

GUIGNET, A. (1981) Etude descriptive d'une population à haut risque: Les suicidants à la prison de préventive genevoise de Champ-Dollon du ler octobre 1977 au 31 mars 1979. *Doctoral thesis*. Faculty of Medicine, University of Geneva.

GUNN, J. (1986) The role of psychiatry in prisons and the right to punishment. In *Psychiatry, Human Rights and the Law* (eds M. Roth & R. Bluglass). Cambridge: Cambridge University Press.

——, ROBERTSON, G., DELL, S., *et al* (1978) *Psychiatric Aspects of Imprisonment*. London: Academic Press.

HARDING, T. W., (1984) Depression en milieu carcéral. *Psychologie Médicale*, 16, 835–839.

HATHAWAY, S. R. & MCKINLEY, J. C. (1981) *Inventaire Multiphasique de Personnalité (M.M.P.I. et la version MINIMULT)*. Paris: Les Editions du Centre de Psychologie Appliquée.

HOLMES, T. H. & RAHE, R. H. (1967) The social readjustment rating scale. *Journal of Psychosomatic Research*, 12, 213–218.

LAZARUS, R. S. (1981) The stress and coping paradigm. In *Models for Clinical Psychopathology* (eds C. Eisendorfer *et al*), pp. 177–213. New York: Spectrum.

MECHANIC, D. (1978) Effects of psychological distress on perceptions of physical health and use of medical and psychiatric facilities. *Journal of Human Stress*, 4, 22–32.

THOITS, P. A. (1982) Conceptual, methodological and theoretical problems in studying social support as a buffer against life stress, *Journal of Health and Social Behaviour*, 23, 145–159.

ZIMMERMANN, E. (1988) Attentes et réalité des soutiens pendant la détention préventive à la prison genevoise de Champ-Dollon, *Déviance et Société*, 12, 361–380.

—— & VON ALLMEN, M. (1985) Consultations médicales et consommations médicamenteuses en cours de détention préventive à la prison de Champ-Dollon. *Médecine Sociale et Préventive*, 30, 312–321.

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Epidemiology of Mental Disorders in Young Adults of a Newly Urbanised Area in Khartoum, Sudan

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Two hundred and four subjects, 22–35 years old, were selected from a surburban part of Khartoum. They were assessed using the Self-Rating Questionnaire, the Eysenck Personality Inventory, and a Sudanese rating scale of anxiety and depression. Socio-economic information was collected. A psychiatric interview and a medical examination were carried out. It was found that 40.3% had at least one psychiatric symptom, and 16.6% received clinical diagnoses according to DSM–III. The most common diagnoses were depressive illness (neurotic and endogenous) (8.4%) and generalised anxiety (3.4%). Alcohol abuse was very rare (0.4%). There was no sex difference.

There is a strong need for epidemiological studies in the field of mental health in developing countries. We are still far from knowing the incidence, prevalence and demographic distribution of various mental disorders in normal populations outside Western culture. The present paper attempts to estimate psychiatric morbidity in the young adult population (22–35 years) of a suburban area of Khartoum, Sudan.

The Hag Yousif area is a newly urbanised locality. Only two decades ago it was a typical traditional rural community of three adjacent villages outside the city of Khartoum. At the time of the present study the population was about 40 000. Of these, 38% were the old indigenous dwellers and 62% were newcomers. Most of the latter group had resided in the area five years or less. Detailed demographic and sociocultural characteristics of this population have been reported by us earlier (Cederblad & Rahim, 1986).

Method

Two random samples totalling 204 adults – 108 males, 96 females – in the age range 22–35 years were selected. *Sample A* represents the indigenous population and comprises 104 subjects previously randomly selected and investigated by one of us in 1964–65 when they were children 3–15 years old (Cederblad, 1968). *Sample B* represents newcomers and comprises 100 subjects drawn randomly from a fresh population census of the area (Department of Statistics, 1984). There was a drop-out rate of 15%: temporary absence from the area was the usual cause. On average, 15% of the data were missing from the various parts of our investigation. These data were critically reviewed and found to be free of any systematic bias that could depreciate the representative nature of the random samples. Hence, percentages were readjusted and computed on valid observations. Percentages from the two samples were then weighted according to the proportions of subjects in the two samples, and estimates representative of the whole population of young adults were thus computed.

Procedure

Each individual was interviewed four times. The first interview was conducted by qualified and trained clinical social workers from the Department of Psychiatry, Clinic for Nervous Disorders, Khartoum North. The second interview was carried out by qualified and trained clinical psychologists from the same department. These two interviews covered all important personal, family, socioeconomic and cultural aspects of the individual's past and current life, as well as a wide range of psychometric batteries including the Eysenck Personality Inventory (EPI; Eysenck & Eysenck, 1964), Raven's Progressive Matrices Test (Raven, 1960), Goodenough's Draw-a-man test (Goodenough, 1926), Well-Being Scale (Beiser, 1974), Life Events Scale (Theorell, 1982; Cederblad & Höök, 1980), Daily Activities Scale (Brenner & Arnetz, 1983), Loneliness Scale (Russel *et al*, 1980), Interview Schedule for Social Integration (ISSI; Henderson *et al*, 1980), Self-Rating Questionnaire (SRQ; Harding *et al*, 1980), and the Rahim Anxiety–Depression Scale (RADS; Rahim, 1973). All investigation instruments were translated into Arabic. The translation was then checked by retranslation into English. The SRQ, EPI and RADS had already been used in Arabic translation in previous Sudanese studies (Rahim, 1973; Harding *et al*, 1980). Since the subjects were semi-illiterate, all information was acquired through interviewing. The subjects' answers were recorded by the interviewer on the relevant forms.

Medical assessment consisted of a general urine analysis, stool examination, and blood tests for haemoglobin concentration, white blood cell count and blood film for malaria. Two general practitioners conducted the medical interview and a clinical examination of all subjects.

Psychiatric assessment was carried out by a senior psychiatrist, who interviewed and examined each individual and made his clinical psychiatric assessment independently of other interviews and data. Psychiatric diagnoses were made according to DSM–III categories (American Psychiatric

Association, 1980). Conditions were judged to be mild, moderate or severe. Those registered as moderate or severe were judged to be similar in nature and degree to the average case with the same diagnosis seen in routine psychiatric outpatient practice in Sudan (Rahim, 1976).

Statistical processing

Data have been analysed using the χ^2 test, Pearson's correlation coefficient (r), and multivariate analysis.

Results

Psychiatric assessment

It was found that 40.3% of the studied adults had at least one psychiatric symptom. In 23.7% the complaints were mild, subclinical, but in the remaining 16.6% they were moderate to severe symptoms that warranted a clinical diagnosis. The nosological breakdown of these cases according to DSM-III categories showed the following: depressive illness (neurotic and endogenous) 8.4% of all subjects, generalised anxiety 3.4%, somatoform disorder 2.4%, conversional reactions 0.7%, psychogenic pain syndrome 0.7%, alcohol abuse 0.4%, and severe mental retardation 0.4%. In Axis II of DSM-III, schizoid personality disorder was diagnosed in 0.7% and borderline personality disorder in 0.4%.

The mild, subclinical psychiatric complaints belonged in the following categories: 7.5% depression, 10.6% generalised anxiety, 3.1% somatoform disorder, 1.2% sexual complaints, 0.9% mild mental retardation and 0.4% alcohol abuse.

Sex. There were no statistically significant sex differences in the prevalence of mental disturbances.

Occupation. Psychiatric morbidity was found to be significantly lower among those engaged in traditional occupations (agriculture and manual labour) than among those in modern occupational sectors (26.2% and 42.2% respectively) ($P<0.05$). Psychiatric symptoms were also more common in those who had stable occupations (35.1%) than in those who were engaged in unstable work such as day-to-day self-employment (22.2%) ($P<0.05$).

Marital status. There was no statistically significant difference between single and married people. However, subjects who reported marital discord and divorce had a significantly higher rate of psychiatric morbidity (37.5%) than those who were married without conflicts or divorce (10.5%) ($P<0.05$).

Life events. Those who cited higher scores of life events showed significantly more psychiatric symptoms (65.4%) than those with medium or low life events scores (33.8% and 34.5% respectively) ($P<0.05$).

Loneliness. The frequency of psychiatric complaints correlated positively with the degree of social isolation as measured by the loneliness scale. Thus those with a high loneliness score had a 54.3% frequency of psychiatric symptoms and those with minimum loneliness score had only 20.5% ($P<0.01$).

Self-Rating Questionnaire

The SRQ score had a strong, positive correlation with the psychiatric assessment ($r=0.69$, $P<0.001$). Highest scores on the SRQ were found in association with a high life events score ($P<0.01$), high loneliness index ($P<0.001$), and marital discord or divorce ($P<0.01$).

Rahim Anxiety–Depression Scale

The RADS score showed a strong positive correlation with the psychiatric assessment ($r=0.71$; $P<0.001$). As with the SRQ, high scores on the RADS were obtained in association with a high life events score ($P<0.05$), high loneliness index ($P<0.01$), and marital discord or divorce ($P<0.01$).

Somatisation scale (RADS–SRQ)

The somatisation scale covers 19 physical symptoms frequently reported in Sudan by patients suffering from anxiety and/or depression (Rahim, 1973). The scale strongly correlated with psychiatric assessment ($r=0.63$, $P<0.001$). Highest scores of somatisation were found in association with a high loneliness index ($P<0.001$), and marital discord or divorce ($P<0.05$).

Neuroticism score

The EPI neuroticism score showed a strong positive correlation with psychiatric assessment ($r=0.53$, $P<0.001$). A high neuroticism score was also found in association with a high loneliness index ($P<0.001$), high life events score ($P<0.001$), and marital discord or divorce ($P<0.05$).

Well-being scale

Psychological well-being did not correlate with psychiatric assessment ($r=0.05$). Individuals who had high life events scores reported lesser degrees of psychological well-being than others ($P<0.05$). We found a better level of well-being in subjects with seasonal rather than stable occupations ($P<0.05$), with fluctuating rather than stable incomes ($P<0.05$), with medium rather than low or high income levels ($P<0.05$), and with a high level of social integration ($P<0.05$).

Discriminant analyses using the psychiatric interview results as the dependent variable showed that a canonic correlation of 0.55 ($P<0.001$) was obtained by combining the state of somatic health, the upper-arm circumference (measure of present nutritional state), income stability, number of life events, loneliness index and two factors from ISSI – 'friendship' and 'social integration'.

Discussion

The high correlations between the results of the psychiatric interview and the self-rating inventories SRQ, EPI and RADS is a validation.

It is difficult to compare investigations made with different methods. Self-rating questionnaires generally give higher frequencies than clinical assessments (Goldberg & Huxley, 1980). Our figure, 16.6% psychiatric cases, can be compared with the results from studies performed in Europe, USA and Australia using clinical interviews, where frequencies vary between 9% and 19.3% (Goldberg & Huxley, 1980). Thus our results are within the range found in various settings in Western culture.

We have no previous reliable data on adults in this area prior to urbanisation. But in a previous study we have shown that while children of this area had a low incidence of behavioural symptoms in 1964–65 (Cederblad, 1968), the following generation of children of the same age and sex distribution in 1980–81 showed a significant increase in behaviour and conduct disorders. In those studies the psychiatric conditions of the parents were only touched upon by two simple questions to the mother: "Are you often nervous or depressed?" and "Is your husband often nervous or depressed?" While 30% of the mothers and 15% of the fathers were reported to suffer from such symptoms in 1964–65, 40% of the mothers and 23% of the fathers were reported to do so in 1980–81. A tentative interpretation of this could be that both children and adults were reported to have fewer psychiatric symptoms in the rural, traditional situation than in the present one of rapid social change. This was expected. Dohrenwend & Dohrenwend (1974), reviewing and summarising data, concluded that eight out of ten studies reported a higher frequency of mental disorder in urban populations than in rural ones, the increase being mainly in neuroses and personality disorders. According to our child study data, the individual most likely to develop behavioural disorder was a school-age boy belonging to the family of a blue-collar wage-earner who had recently immigrated from a rural area and had a poor income, low living standard, and an overcrowded home (Rahim & Cederblad, 1986). Data from the present study seem to confirm the findings from our child study. In both there is a higher rate of mental symptoms in those most exposed to the stress of modern life, particularly blue-collar workers with stable but rather unsatisfactorily paid jobs.

Loneliness was found to be associated with a significantly higher frequency of mental symptoms. But feelings of loneliness could be an expression of uprootedness, isolation and lack of social support. This is what frequently happens to rural folk when they migrate to urban centres away from their extended family and cohesive rural community.

In short, most of the variables found to be associated with an increased frequency of mental symptoms were of the type which is more common in urban than in rural settings: modern-sector occupations with stable, monthly salaries and a stable, unsatisfactory income, loneliness, marital discord or divorce, and excessive life changes. Comparisons between the two subsamples to elucidate the impact on mental health of growing up in an area during a period of rapid social change (as in the case of the indigenous sample) or of rural–urban migration (as in the case of the newcomers) will be reported in another paper.

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References

American Psychiatric Association (1980) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn). Washington DC: APA.

Beiser, M. (1974) Components and correlates of mental well-being. *Journal of Health and Social Behaviour*, **15**, 320–327.

Brenner, S-O. & Arnetz, B. (1983) Effekter av otrygghet i arbetet, förlust av arbetet och arbetslöshet: de tre första mätningarna på gruppen arbetsösa som deltar i ett åtgärdspaket. *Stressforskningsrapporter*, no. 170 (in Swedish).

Cederblad, M. (1968) A child psychiatric study on Sudanese Arab children. *Acta Psychiatrica Scandinavica*, **44**, Suppl. 200.

—— & Höök, B. (1980) Daghemsvård för treåringar: en tvärvetenskaplig, experimentell studie – X. Sammanfattning. *Reports from the Laboratory for Clinical Research on Stress, Karolinska Institute, Stockholm*, no. 121 (in Swedish).

—— & Rahim, S. I. A. (1986) Effects of rapid urbanization on child behaviour and health in a part of Khartoum, Sudan – I. Socio-economic changes 1965–80. *Social Science and Medicine*, **22**, 713–721.

Department of Statistics, Sudanese Government (1984) *Population Census in Sudan*. Khartoum: Government Press.

Dohrenwend, B. P. & Dohrenwend, B. S. (1974) Social and cultural influences on psychopathology. *Annual Review of Psychology*, **25**, 417–452.

Eysenck, H. J. & Eysenck, S. B. G. (1964) *Manual of the Eysenck Personality Inventory*. London: University of London Press.

Goldberg, D. & Huxley, P. (1980) *Mental Illness in the Community*. London, New York: Tavistock Publications.

Goodenough, F. L. (1926) *Measurement of Intelligence by Drawings*. Yourkers-on-Hudson, NY: World Book Co.

Harding, T. W., de Arango, M. V., Baltazar, J., *et al* (1980) Mental disorders in primary health care: a study of their frequency and diagnosis in four developing countries. *Psychological Medicine*, **10**, 231–241.

Henderson, P., Duncan-Jones, P., Byrne, D. G., *et al* (1980) Measuring social relationship: the interview schedule for social interaction. *Psychological Medicine*, **10**, 723–734.

RAHIM, S. I. A. (1973) Anxiety–depression rating scale tested in a large clinical sample. *Proceedings of 3rd Pan African Psychiatric Conference, Khartoum.*

—— (1976) Epidemiology of neurosis in Sudan. *African Journal of Psychiatry*, **1**, 21–31.

RAHIM, S. I. A. & CEDERBLAD, M. (1986) Effects of rapid urbanization on child behaviour and health in a part of Khartoum, Sudan – II. Psychosocial influences on behaviour. *Social Science and Medicine*, **22**, 723–730.

RAVEN, J. C. (1960) *Guide to the Standard Progressive Matrices*. London: H. K. Lewis & Co.

RUSSELL, D., PEPLAU, L. A. & CUTRONA, C. E. (1980) The revised UCLA loneliness scale: concurrent and discriminant validity evidence. *Journal of Personality and Social Psychology*, **39**, 472–480.

THEORELL, T. G. T. (1982) Advances in cardiology: psychological problems before and after myocardial infarction. *Review of Research on Life Events and Cardiovascular Illness*, **29**, 140–147.

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DSM-III Major Depressive Disorder in the Community

A Latent Class Analysis of Data from the NIMH Epidemiologic Catchment Area Programme

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The fit of the structure of DSM-III major depressive disorder to data from two large epidemiological surveys is assessed by latent class analysis. The surveys were conducted at the Baltimore and Raleigh-Durham sites of the National Institute of Mental Health (NIMH) Epidemiologic Catchment Area Program. Three classes are required to fit the data, and the third class bears a strong resemblance to major depressive disorder, although it requires slightly more symptoms to be present than DSM-III. The derived structure replicates successfully for Baltimore and Raleigh-Durham, with a prevalence of the major depression category of 0.9% for both sites.

Empirical evidence for the manner in which signs and symptoms cluster into purported diagnostic categories has been termed *internal construct validity* by Young (1983). Although there is considerable logic in favour of quantitative studies of the taxonomy of psychiatric disorders such as depression (e.g. as Pfohl and Andreasen argue in their 1978 paper), by 1976 the results were so ambiguous that Kendell could state that ". . . the forty or so factorial studies of depressive symptomatology that have been performed in the last twenty years leave us little the wiser" (1976, p. 21). Many of the studies reviewed by Kendell were factor analyses and cluster analyses conducted in the late 1960s and early 1970s (e.g. Eysenck, 1970; Paykel, 1971; Everitt *et al*, 1971; Fleiss, 1972). Reviewing much of the same evidence in 1982, Andreasen was slightly more positive in concluding that the studies "give some mathematical validation to at least one traditional subtype (the severe, psychotic, or endogenous)".

Several new methods of quantitative classification have been developed since these research studies and reviews were conducted, including dichotomous factor analysis (Muthen, 1978), latent trait analysis (Duncan-Jones *et al*, 1986), grade of membership analysis (Woodbury *et al*, 1978), multidimensional scaling (Schiffmann *et al*, 1981) and latent class analysis (McCutcheon, 1987). All these methods have important advantages over standard factor and cluster analysis (for an overview, see Everitt, 1984 or Bartholomew, 1987). Although we cannot present a comparison of advantages and disadvantages of these methods, which collectively we term latent structure models, we will present and discuss several important advantages of the method used here, latent class analysis.

One important weakness in almost all studies of the internal construct validity of depressive disorders is that the data on signs and symptoms were obtained from patients being treated in psychiatric settings. Although psychiatric epidemiologic surveys have been conducted for at least a century, the data obtained have been insufficient for numerical taxonomic analysis. In some cases symptom checklists have been obtained from community samples (e.g. Radloff, 1977), but the resulting data do not provide an adequate breadth of coverage of psychopathology to be informative about the specific categories of affective disorders. In some epidemiologic studies there has been adequate information to make diagnoses, but the material on signs and symptoms has not been retained to allow empirical study of the covariance of signs and symptoms.

This feature of research on depression – that empirical taxonomic studies are conducted on samples of patients – is not trivial. In deciding how to formulate a diagnostic category, the relevant base for the formulation should be the entire population, not the treated population. There are presumably important and strong selection biases for treatment for depression, as there are for most illnesses. In all probability, treated cases have more signs and symptoms than untreated cases, and the signs and symptoms they have are more severe. It also seems likely that treated cases have more psychopathology and physical illness outside the area of depression. Although these biases have not yet been conclusively established, they are so reasonable as to vitiate the value of the study of internal construct validity with samples of treated cases.

In this analysis we take advantage of data from the NIMH Epidemiologic Catchment Area (ECA) Program. These data are unique in including reports, from large community samples, on symptoms explicitly related to the diagnostic category of major depressive disorder, as laid out in DSM-III (American Psychiatric Association, 1980). Thus, our major research question here is: can we 'give some mathematical validation' to the most important and traditional subtype (major depressive disorder), with improved methods of classification and data from community samples?

The Epidemiologic Catchment Area Program

The Epidemiologic Catchment Area (ECA) Program is a series of epidemiological surveys conducted by university-based researchers in five community mental health centre catchment area populations (Eaton *et al*, 1981). At each site interviews were conducted with probability samples of about 3000 individuals living in the household population and about 500 individuals living in institutions. Each site included at least two rounds of interviews separated by one year. The research design is described in Eaton *et al* (1981) and in Eaton & Kessler (1985). Data presented below are drawn from the household sample of the Johns Hopkins ECA site in Baltimore, Maryland, and the Duke site in Raleigh-Durham, North Carolina.

The first wave of household interviewing yielded 3481 completed interviews in Baltimore for a response rate of 78%, and 3921 in Raleigh-Durham, with a 77% response rate. Initial analyses of data on non-response (Von Korff *et al*, 1985) do not reveal strong biases among sociodemographical or psychopathological variables according to non-response or attrition status. There were complete data on all relevant symptoms on 3198 subjects in Baltimore and 3614 subjects in Raleigh.

The section of the interview on psychopathology common to all the ECA sites was drawn from the NIMH Diagnostic Interview Schedule (DIS) (Robins *et al*, 1985). The DIS is a highly structured interview designed to resemble a typical psychiatric interview and to yield similar results in terms of specific mental disorder diagnoses. Results of a study of inter-rater agreement of the DIS conducted with a sample of patients in a clinical setting produced moderately good estimates of test–retest concordance for diagnoses (Robins *et al*, 1981).

Latent Class Analysis

In their classic discussion Lazarsfeld & Henry (1968) define a latent variable as an unobserved variable that explains the association among a set of observed variables. This definition is consistent with the notion of a 'factor' in factor analysis, which is estimated so as to minimise covariation among observed variables, after adjusting for the factor score. The approach in factor analysis assumes that variables are normally distributed and related to each other in a linear and additive fashion. In latent class analysis the variables are assumed to be categorical in nature, and there are no assumptions of linearity or additivity.

Observed covariation among categorical variables can be analysed by an n-way cross-tabulation, where n is the number of observed variables. In such a cross-tabulation, a standard Pearson χ^2 test of departure from independence states whether there is association among the variables. If there is association, there might exist some other variable X, with, say, T classes, such that the association in the n-way cross tabulation was zero or trivial within each class of X. If X is observable, it may be concluded that it has explained the association among the n variables, according to the standard logic of survey analysis (Rosenberg, 1968). If X is not observable, it meets the definition of the latent variable set forth by Lazarsfeld & Henry (1968).

In latent class analysis, iterative fitting algorithms such as were developed by Goodman (1974) and Clogg (1977) seek latent variables that are successful in eliminating or reducing within-class association among observed variables. Use of the likelihood ratio χ^2 yields a statistical measure of the goodness of fit. The analysis yields two sets of important parameters. One set of parameters is the proportion in the sample in the various T classes of the unobserved X variable. In the epidemiological framework these parameters are prevalences. Another set of parameters is the set of probabilities that the observed variables take values, given that the individual is a member of an unobserved class. Clogg (1979) has suggested that these conditional probabilities are similar to the concept of factor loadings in factor analytic models.

There is a confirmatory aspect to latent class analysis. By requiring that certain conditional probabilities equal unity or zero (referred to as deterministic constraints), explicit relationships can be incorporated into the analysis. Conditional probabilities in different classes can also be constrained to equal one another (equality constraints). Thus, a given diagnostic model can be tested in a confirmatory mode. The question of interest becomes: if the sample is divided into those subjects meeting criteria for diagnosis and those not meeting criteria, is the association of the symptom variables reduced to a non-significant level?

Latent class analysis has certain important advantages over traditional factor analysis. It does not require or assume that the data are normally distributed, which is rarely or ever true in the case of psychopathology. Moreover, the measures of the association used are based on the odds-ratio, which means that they are not influenced by the prevalence of the characteristic under study. Thus, taxonomic results can be compared for samples which differ in their prevalence (e.g. samples of men and women; samples of subjects under treatment against those in the community). Finally, there is no assumption of additivity in the association between variables. Since many diagnostic categories may not necessarily conform to dimensional concepts, this advantage of latent class analysis is a crucial one.

Results

First the prevalence of individual symptoms and DSM–III symptom groups is described. In the DIS, the phrasing of all symptom questions is in the lifetime format, beginning with the phrase "Have you ever? . . ." If the answer is positive, questions follow to ensure that the symptom meets criteria of severity, and that it was not caused by drugs, medication, alcohol, physical illness, or injury. If these conditions are met, the symptom is considered to be a "plausible psychiatric symptom" (Robins *et al*, 1985). After all symptoms in the general area of depression are enquired about, the respondent is asked whether the symptoms ever occurred together, and if so, whether they were dysphoric during that particular time. Then, there are questions on the first and most recent occurrence of 'these problems'. The symptom data can be used to analyse the lifetime prevalence of DSM–III major depressive disorder (Robins *et al*, 1984).

There are anomalies in the analysis of lifetime prevalence data that lead us to be very cautious about their interpretation and analysis. For example, the lifetime prevalence of major depressive disorder declines with increase in age (Robins *et al*, 1984), which indicates either a high mortality rate, or a large cohort effect, or a tendency for older persons to forget or deny symptoms which have occurred in the distant past. These problems led us to focus on the symptoms occurring within the month prior to the interview. This was made possible by the implementation of probes for recall of symptom occurrence used in several of the ECA sites (Von Korff & Anthony, 1982). Since this information is available for every symptom, there is little possibility of error due to failure to recall the timing and clustering of the individual symptoms in a given episode.

Table I presents data on the prevalence of the DIS symptoms relevant to major depressive disorder and the prevalence of the DSM–III symptom groups for all respondents in Baltimore. The table presents abbreviated descriptions of the DIS questions – most of them include several phrases relevant to the symptom in question, and almost all include the phrase "a period of two weeks or more when you. . .". For example, DIS Question 72, which is the indicator for DSM–III criterion A, is worded as follows: "In your lifetime, have you ever had two weeks or more in which you felt sad, blue, depressed, or when you lost all interest and pleasure in things that you usually cared about or enjoyed?" This symptom is referred to in the table 'dysphoria'. As described above, the symptoms are recorded as having been present in the month prior to the interview, having met the DIS criteria of severity, and, where appropriate, causes of the symptom due to medication, drugs, alcohol, physical illness, or injury have been ruled out according to the DIS method (Robins *et al*, 1985). The group prevalences record the presence of any symptom in the group, according to the same criteria, so that these prevalences are constrained to be equal to or greater than the symptom prevalences.

TABLE I

Prevalence of dysphoria and eight DIS/DSM–III symptom groups for all respondents in the Epidemiologic Catchment Area of East Baltimore

Symptom or group title, DIS no. and content of DIS question	*Percentage prevalence of symptom*	*Percentage prevalence of any symptom in the group*
Dysphoria		4
72 Sad for 2 weeks	4	
Group 1		6
74 Loss of appetite	2	
75 Lose 2 lbs/week	1	
76 Gain 2 lbs/week	4	
Group 2		11
77 Trouble falling asleep	9	
78 Sleeping too much	2	
Group 3		6
80 Talk/move slowly	3	
81 Move all the time	3	
Group 4		2
82 Loss of interest in sex	2	
Group 5		7
79 Tired out	7	
Group 6		3
83 Worthless	3	
Group 7		5
84 Trouble concentrating	4	
85 Thoughts slow	3	
Group 8		9
86 Thought about death	8	
87 Wanted to die	3	
88 Thought of suicide	1	
89 Attempted suicide	0	

The most frequent symptoms are 'trouble falling asleep' (9%), 'thought about death' (8%), and 'tired out' (7%). Only one symptom, 'attempted suicide', had a prevalence which rounded to zero. In some symptom groups the overlap of symptoms is already apparent: for example, in groups 7 and 8, the prevalence of the group is only slightly higher than the most prevalent symptom. In other groups the substitutability of the symptoms is apparent: for example, in groups 2 and 3, respondents tend to have one or the other symptom, but not both, so that the group prevalence is the sum of the symptom prevalences.

TABLE II

Dysphoria and eight DIS/DSM-III symptom groups: most frequent combinations of data for all respondents in the Epidemiologic Catchment Area of East Baltimore

Cell number	*Frequency*	*Cumulative percentage*	*DIS/DSM-III symptom groups in which symptoms occurred*[1]
1	2393	74.8	No symptoms
129	122	78.7	2
3	107	82.0	8
17	52	83.6	5
257	50	85.2	1
65	29	86.1	3 8
5	30	87.0	7
131	21	87.7	2 8
385	16	88.2	1 2
145	15	88.7	2 5
2	14	89.1	D
33	14	89.6	4
67	11	89.9	3 8
81	10	90.2	3 5

1. D dysphoria; 1 appetite loss or weight change; 2 insomnia or hypersomnia; 3 psychomotor agitation or retardation; 4 loss of interest; 5 fatigue; 6 feelings of worthlessness; 7 concentration problems; 8 suicidal ideation.

How might these symptoms be grouped in the population? With eight groups and dysphoria, there are two to the ninth power or 512 possible patterns of responses. Table II shows that, next to no symptom groups at all (cell one with 75% of the sample), the most frequent response patterns are the occurrence of a single symptom group. Seven patterns (no symptoms; group 2 only; group 8 only; group 5 only; group 1 only; group 3 only; and group 7 only) account for 87% of the sample. Another 7% are accounted for by five patterns showing the occurrence of two symptom groups only, and two more patterns with one symptom only. Thus, out of 512 possibilities, 14 patterns account for 90% of the sample.

Of the 512 possible patterns, 256 do not include dysphoria and will, therefore, not be eligible for meeting DSM-III criteria for a major depressive episode. Of the 256 patterns which include dysphoria, combinatorial logic shows that 163 meet DSM-III criteria and 93 do not. The figure 163 is the sum of the possible combinations of eight things taken eight at a time (1); seven at a time (8); six at a time (28); five at a time (56); and four at a time (70). How frequently do these patterns occur in the sample?

TABLE II

Dysphoria and eight DIS/DSM-III symptom groups: combinations of data meeting criteria for DSM-III major depressive disorder, in order by frequency for all respondents in the Epidemiologic Catchment Area of East Baltimore

Cell number	*Frequency*	*DIS/DSM-III symptom groups in which symptoms occurred*							
480*	3	1	2	3		5	6	7	8
352*	3	1		3		5	6	7	8
454	3	1	2	3				7	
472*	2	1	2	3		5		7	8
408*	2	1	2			5		7	8
256*	2		2	3	4	5	6	7	8
212	2		2	3		5			8
512*	1	1	2	3	4	5	6	7	8
502*	1	1	2	3	4	5		7	
498*	1	1	2	3	4	5			
496*	1	1	2	3	4		6	7	8
478*	1	1	2	3		5	6	7	
468*	1	1	2	3		5			8
462*	1	1	2	3			6	7	
456*	1	1	2	3				7	8
416*	1	1	2			5	6	7	8
400*	1	1	2				6	7	8
398*	1	1	2				6	7	
350*	1	1		3		5	6	7	
348*	1	1		3		5	6		8
248*	1		2	3	4	5		7	8
224*	1		2	3		5	6	7	8
220*	1		2	3		5	6		8
216*	1		2	3		5		7	8
214*	1		2	3		5		7	
200*	1		2	3				7	
160*	1		2			5	6	7	8
144*	1		2				6	7	8
84*	1			3		5	6	7	
88*	1			3		5		7	8
482	1	1	2	3	4				
466	1	1	2	3		5			
452	1	1	2	3					8
396	1	1	2				6		8
406	1	1	2			5		7	
242	1		2	3	4	5			
180	1		2		4	5			8
152	1		2			5		7	8
92	1			3		5	6		8
Total number of									
cells	39	23	33	29	9	28	19	27	26
cases	49	31	41	38	10	36	24	36	34

*Cell assigned to class C of restricted (C) model in Table IV.

Table III shows all combinations of symptom groups meeting DSM-III criteria for major depressive disorder which actually occurred in the sample, in order of frequency of occurrence. Of the 163 possible combinations, only 39 actually occurred in the sample. There were 49 cases in this sample, for a prevalence of DIS/DSM-III depressive disorder of 1.5%. Several symptom groups are relatively more common among these 49 DSM-III cases, including groups 2 (sleep problems – 41 cases) and 7 (concentration – 36 cases). Two groups are much less common: loss of pleasure, present in 10 cases; and feelings of worthlessness, present in 24 of the 49 cases.

The cross-tabulation of every symptom group (including dysphoria) with every other group produced a 512-cell table which was submitted to the Maximum Likelihood Latent

TABLE IV

Latent class analysis of model fitting results for data on depression for the Epidemiologic Catchment Area of East Baltimore

Model	χ^2	*Degrees of freedom*	*Class prevalence*			
			A	*B*	*C*	*D*
Independence	2416	511				
Two classes						
Unrestricted	559	492	88	12	–	–
Restricted (DSM–III)	1045	493	97	3	–	–
Three classes						
Unrestricted	400	482	83	15	2	–
Restricted (C)	436	483	86	12	1	–
Restricted (BC)	995	485	97	2	1	–
Four classes						
Unrestricted	376	474	82	14	2	2
Restricted (C)	385	473	82	15	1	2

Structure Analysis Program (Clogg, 1977) as described above. (The programme had to be re-dimensioned to accept so large a table.) Table IV reports the results of several latent class analyses of these data.

The model of independence produces a large χ^2 value of 2416, indicating that there is a substantial amount of covariation among the symptoms groups. If we require the algorithm to fit a model with just two classes, a large amount of that covariation is explained – χ^2 for this unrestricted model is 559, with 492 degrees of freedom. This fit is surprisingly effective but nevertheless unacceptable because χ^2 is too large. Examining the conditional probabilities in this model (not shown) reveals class A to be the 'normal' population, since the probabilities are so low for those in their class. Class B is the 'depressives', comprising 12% for the sample. If we place a restriction in the model to require that dysphoria be present in the class of 'depressives', in effect mimicking the structure of DSM–III, χ^2 is increased to 1045, even though the prevalence of 3% is in accord with common wisdom. If the restricted two-class model fits the data well (e.g. with χ^2 below 500), that would mean that all the covariation in these symptom groups could be explained by the simple presence or absence of a single disorder – a strict, simple, and elegant model.

An unrestricted three-class model fits the data fairly well, with a χ^2 value of 400. The class of 'normals' has a prevalence of 83%, and there is a third class (C) which includes severely depressed individuals with high conditional probabilities of symptom occurrence, at a prevalence of 2%. The intermediate class B has a prevalence of 15%. The second three-class model is a restricted model and is labelled 'C' because dysphoria is constrained to be present in class C. This model represents the closest approximation to the diagnostic structure in DSM–III and it is therefore discussed in more detail after an examination of the fit of the single remaining three-class model and certain four-class models. A final three-class model labelled 'restricted – BC' constrains dysphoria to be present in both of the depressive classes. The fit is unacceptable with a χ^2 value of 995.

Two four-class models were tested and they fit the data acceptably. The unrestricted four-class model produced a χ^2 value of 376. There are two 'severe' classes in this model with prevalence of 2% each, and an intermediate class with prevalence of 14%. A four-class model with dysphoria constrained to be present in the third class also fits the data well. But in neither of these models was there an important improvement in fit over the three-class models, and since they are less parsimonious, we focus on the three-class restricted model.

The value of χ^2 in this circumstance is somewhat compromised as a test of fit because of the large number of cells in the table with expected frequencies less than five. The impact is to overestimate the effective degrees of freedom, and be less likely to reject the fit. Where models are hierarchical, and χ^2 values with degrees of freedom are obtained by subtraction, this problem is less threatening. Therefore we are somewhat cautious about the overall fit, but impressed with the significant improvement in fit of the three-class restricted (C) model over the three-class unrestricted model. These two models are hierarchical, so that the appropriate value of χ^2 is 36 with one degree of freedom.

Table V presents the probabilities for positive responses, conditional on class membership, associated with the three-class model of interest (restricted – C). The probability of 1.0 for dysphoria signifies the restriction that it always be present, consistent with DSM–III structure. Other probabilities are also quite high, with the exception of loss of interest in sex. Class C is a slightly more conservative definition of depression than the DSM–III, in that every single response pattern which belongs within class C is consistent with the definition of DSM–III. This inclusion is denoted by an asterisk by the cell number in Table III. All response patterns with dysphoria and *five* or more symptom groups are included in class C (and in DSM–III major depressive disorder). But certain response patterns with dysphoria and *four* symptom groups are in DSM–III and not in class C (patterns 454, 212, 482, 466, 452,

TABLE V

Latent class analysis for a three-class model with dysphoria constrained to be present in the third class: conditional probabilities for positive responses for the Epidemiologic Catchment Area of East Baltimore

DSM–III group	*Class*		
	I	*II*	*III*
Dysphoria	0.004	0.192	1.000
Group 1 – Weight	0.019	0.283	0.648
Group 2 – Sleep	0.045	0.475	0.779
Group 3 – Slow	0.009	0.314	0.778
Group 4 – Sex	0.005	0.129	0.171
Group 5 – Tired	0.017	0.379	0.764
Group 6 – Worthless	0.002	0.153	0.603
Group 7 – Concentration	0.010	0.256	0.873
Group 8 – Death	0.041	0.357	0.744

396, 406, 242, 180, 152, 92). All but one of these patterns include group 2 (problem sleeping). This suggests that problems in sleeping may be an indicator of a less serious form of disorder – a disorder which does not necessarily include dysphoria. There are also certain response patterns with less than five symptom groups which are potent enough to place them in class C. These include patterns 398, 214, 144, 94, and 88. All these patterns include group 7 (concentration). This suggests that concentration problems may be an indicator of a more serious form of depressive disorder.

Class B includes a variety of response patterns from the same domain of content. The most probable symptom is group 2 (problems with sleep), but thoughts about death, feeling tired, and motor activity are all also fairly probable. Dysphoria is only present in about 20% of the cases.

The method of latent class analysis allows strict comparison of taxonomic structures between different groups in the population. Here, to assess the robustness of the findings in Table V, a comparison has been made with data from the Raleigh-Durham site of the ECA Program. A model was fitted to the data from both sites simultaneously, in order to examine how similar the structures were. The conditional probabilities in the model for the two sites were so similar that models were fitted to the data requiring that conditional probabilities be equal in the two sites – this equality is called 'structural homogeneity' in the literature on latent class analysis. Thus, for example, the conditional probability of a positive response on DSM–III group 1 (weight–appetite) for those in the third (depression) class was 0.5859 in Baltimore and 0.5859 in Raleigh-Durham; for group 2 (sleep problems) both probabilities were equal to 0.7485 – both quite close to the probabilities shown in Table V for Baltimore only. It was possible to fit a model successfully with only one parameter not constrained to equality in the depression class. The exceptional parameter was for group 6 (feelings of worthlessness), which had a value of 0.6243 in the Baltimore sample and 0.2876 in the Raleigh-Durham sample. In effect, depressives in Baltimore are more likely to feel worthless, sinful, or guilty than those in Raleigh-Durham. It may be that a more useful classification for depression would include this parameter as part of the concept of dysphoria, and not as a separate symptom group.

There were also four parameters in the second class which had to be free to vary between the sites (groups 1, 3, 4, and 7). The estimated values for these parameters, while different, were not widely divergent (e.g. 0.2910 v. 0.1673 for group 1; 0.3135 v. 0.2218 for group 3). Finally, there was one parameter in class I which was allowed to differ – thoughts of death had a probability of 0.0411 in Baltimore for the 'normal' group, and 0.0238 for the 'normal' class in Raleigh-Durham. In all, six of the 27 parameters were unconstrained in the three-class model. Only one of the unconstrained parameters was in the third class.

The prevalences for the classes were allowed to vary, even as the hypothesis of structural homogeneity was being tested. But the prevalence of the third class was 0.0092 in Baltimore and 0.0090 in Raleigh-Durham – or very close to 1% prevalence in both sites. This prevalence is lower than the 3–4% reported in other analyses of ECA data (Myers *et al*, 1984) because we are requiring all symptoms to be present in the month before the interview, and using a slightly stricter definition of depression than the DIS/DSM–III method.

The likelihood ratio χ^2 for the model fitted for data from Baltimore and Raleigh-Durham together was 794.7, with 986 degrees of freedom. It is wise to be cautious in accepting a fit to data as sparse as these are, with many cells having expected frequencies less than unity. But this is a relatively large sample, and even with 200 less degrees of freedom, the observed values and those expected under the model would not differ statistically at the level of 0.05.

Discussion

The experience which generated the DSM–III originated in clinical settings, non population-based samples. Indeed, data from household populations have never been collected in a form which allows such a direct test of a diagnostic model. Class C above is quite close to DSM–III major depressive disorder, although perhaps slightly more severe. This amounts to a statistical and community-based confirmation of the general concept of depressive disorder, if not of exactly the DSM–III algorithm. The robustness of the findings in the comparison with the separate ECA site at Raleigh-Durham is credible, and the near equality of class prevalences is also an important result.

Class B above is some sort of intermediate disorder which does not necessarily involve dysphoria – perhaps the atypical affective disorder labelled type V by Davidson *et al* (1982). We intend to investigate this possibility and others such as dysthymia (APA, 1987), and 'neurotic' depression (Klerman *et al*, 1979) in future analyses.

Certain problems are apparent in the data and the analysis. Loss of interest in sex may be a poor indicator of loss of interest in things usually enjoyed, but it is all that is available in the data, separate from the question on dysphoria. It is not a useful symptom in the data presented above. In the revision to the DSM–III (American Psychiatric Association, 1987), the importance of sexual drive, as an indicator of more generally diminished interest or pleasure, has been de-emphasised. As with our analyses in general, we are constrained to the DSM–III symptoms as operationally defined and measured by the DIS. If the sample were large enough, and the latent structure algorithm robust enough, it would be better to study the covariation in symptoms themselves, instead of coding them into DSM–III symptom groups. But the limits of the data and the algorithm oblige us to use this group structure in the analyses. Finally, we have constrained the analyses to the single domain of depressive symptomatology included in the DIS depression section. Study of the overlap of depression with symptoms of somatisation disorder or anxiety disorders, for example, has not been attempted in this analysis. Other future research of interest includes analyses comparing population subgroups, for example according to gender and age.

This analysis reflects on the internal construct validity of the DSM-III diagnosis of major depressive disorder as measured by the DIS. Other important criteria of validity exist, of course, and all these must be weighted in any ultimate judgement of the utility of this diagnostic category.

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References

American Psychiatric Association (1980) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn) (DSM–III). Washington DC: APA.

—— (1987) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn, revised) (DSM–III-R). Washington DC: APA.

Andreasen, N. C. (1982) Concepts, diagnosis, and classification. In *Handbook of Affective Disorders* (ed. E. S. Paykel). New York: The Guilford Press.

Bartholomew, D. J. (1987) *Latent Variable Models and Factor Analysis*. London: Oxford University Press.

Clogg, C. C. (1977) *Unrestricted and Restricted Maximum Likelihood Latent Structure Analysis: A Manual for Users*. Pennsylvania: State College, Pennsylvania State University.

—— (1979) Some latent structure models for the analysis of likert-type data. *Social Science Research*, 8, 287–301.

Davidson, J. R., Miller, R. D., Turnbull, C. D., *et al* (1982) Atypical depression. *Archives of General Psychiatry*, 39, 527–534.

Duncan-Jones, P., Grayson, D. A. & Moran, P. A. (1986) The utility of latent trait models in psychiatric epidemiology. *Psychological Medicine*, 16, 391–405.

Eaton, W. W., Regier, D. A., Locke, B. Z., *et al* (1981) The NIMH Epidemiologic Catchment Area Program. *Public Health Reports*, 96, 319–325.

—— & Kessler, L. G. (eds) (1985) *Epidemiologic Field Methods in Psychiatry: The NIMH Epidemiologic Catchment Area Program*. New York: Academic Press.

Everitt, B. S. (1984) *An Introduction to Latent Class Models*. London: Chapman & Hall.

——, Gourlay, A. J. & Kendell, R. E. (1971) An attempt at validation of traditional psychiatric syndromes by cluster analysis. *British Journal of Psychiatry*, 119, 399–412.

Eysenck, H. J. (1970) The classification of depressive illness. *British Journal of Psychiatry*, 117, 241–250.

Fleiss, J. L. (1972) Classification of the depressive disorders by numerical typology. *Journal of Psychiatry Research*, 9, 141–153.

Goodman, L. A. (1974) The analysis of systems of qualitative variables when some of the variables are unobservable: Part I – a modified latent structure approach. *The American Journal of Sociology*, 79, 1179–1259.

Kendell, R. E. (1976) The classification of depression: a review of contemporary confusion. *British Journal of Psychiatry*, 129, 15–28.

Klerman, G. L., Endicott, J., Spitzer, R., *et al* (1979) Neurotic depressions: systematic analysis of multiple criteria and meanings. *American Journal of Psychiatry*, 136, 57–61.

Lazarsfeld, P. R. & Henry, N. W. (1968) *Latent Structure Analysis*. Boston: Houghton–Mifflin.

McCutcheon (1987) *Latent Class Analysis*. Beverly Hills: Sage.

Muthen, B. (1978) Contributions to factor analysis of dichotomous variables. *Psychometrics*, 43, 551–560.

Myers, J. K., Weissman, M. M., Tischler, G. L., *et al* (1984) Six month prevalence of psychiatric disorders in three communities. *Archives of General Psychiatry*, 41, 959–970.

Paykel, E. S. (1971) Classification of depressed patients: cluster analysis derived grouping. *British Journal of Psychiatry*, 18, 275–288.

Pfohl, B. & Andreasen, N. C. (1978) Development of classification systems in psychiatry. *Comprehensive Psychiatry*, 19, 197–207.

Radloff, L. S. (1977) The CES-D scale: a self-report depressive scale for research in the general population. *Journal of Applied Psychological Measurement*, 1, 385–401.

Robins, L. N., Helzer, J. E., Weissman, M., *et al* (1984) Lifetime prevalence of specific psychiatric disorders in three sites. *Archives of General Psychiatry*, 41, 949–958.

Robins, L. N., Helzer, J. E., Croughan, J., *et al* (1981) National Institute of Mental Health Diagnostic Interview Schedule. *Archives of General Psychiatry*, 38, 381–389.

Robins, L. N., Helzer, J. E., Orvaschel, H., *et al* (1985) The Diagnostic Interview Schedule. In *Epidemiologic Field Methods in Psychiatry: The NIMH Epidemiologic Catchment Area Program* (eds W. W. Eaton & L. G. Kessler). New York: Academic Press.

Rosenberg, M. (1968) *The Logic of Survey Analysis*. New York: Basic Books.

Schiffman, S. S., Reynolds, M. L. & Young, F. W. (1981) *Introduction to multidimensional scaling: theory, method, and applications*. New York: Academic Press.

Strauss, J. S., Bartko, J. J. & Carpenter, W. T. (1973) The use of clustering techniques for the classification of psychiatric patients. *British Journal of Psychiatry*, 122, 531–540.

Von Korff, M. R. & Anthony, J. C. (1982) The NIMH Diagnostic Interview Schedule modified to record current mental status. *Journal of Affective Disorders*, 4, 365–371.

——, Cottler, L., George, L. K. *et al* (1985) Non-response and non-response bias in the ECA surveys. In *Epidemiologic Field Methods in Psychiatry: The NIMH Epidemiologic Catchment Area Program*. New York: Academic Press.

Woodbury, M. A., Clive, J. & Garson, A. (1978) Mathematical typology – a grade of membership technique for obtaining disease definition. *Computers and Biomedical Research*, 11, 277–298.

Young, M. A. (1983) Evaluating diagnostic criteria: a latent class paragon. *Journal of Psychiatric Research*, 17, 285–296.

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Tardive Dyskinesia in Bipolar Affective Disorder: Relationship to Lithium Therapy

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Forty patients under the age of 60 years with a DSM-III diagnosis of bipolar affective disorder were examined for the presence of tardive dyskinesia. The overall prevalence was 22.5%, with an age-related increase. Patients with and without tardive dyskinesia did not differ in terms of duration of affective illness or exposure to neuroleptics, but those patients with tardive dyskinesia had significantly more psychiatric admissions and were on lithium for significantly greater lengths of time.

Prevalence rates of orofacial dyskinesia in neuroleptic-treated patients vary widely from one study to the next (for review see Kane *et al*, 1984). In a survey of 56 studies a mean prevalence of 20% was found (Kane & Smith, 1982). The most consistently reported risk factor is age, older patients being at greater risk (Waddington & Youssef, 1988). Women are probably at greater risk than men, especially of developing more severe forms of the disorder (Smith *et al*, 1978; Kane & Smith, 1982). Dose–response curves for tardive dyskinesia (TD) have in general not been demonstrated. Waddington & Youssef (1986) could find no relationship between the development of TD and either the duration or vigour of treatment with neuroleptics.

It has been suggested that patients with affective illness are at greater risk of developing TD than are patients with schizophrenia (Kane *et al*, 1980). As a result of this, a monograph published by the American Psychiatric Association recommends that patients with bipolar affective disorder should not be prescribed long-term neuroleptic medication except in rare circumstances (Gardos & Casey, 1984). Lithium, which is widely used in the prophylaxis of bipolar affective disorder, has, however, been reported as effective in the management of TD (Prange *et al*, 1973; Reda *et al*, 1975; Gerlach *et al*, 1975). We decided to examine further the prevalence of tardive dyskinesia in bipolar out-patients, concentrating in particular on differences between patients taking lithium and those for whom it had never been prescribed.

Method

The study population consisted of 40 out-patients aged 30–60 years, all of whom had a DSM-III diagnosis of bipolar affective disorder (American Psychiatric Association, 1980). During the course of their illness, each had been prescribed neuroleptics for at least two months. The diagnosis of bipolar affective disorder was based on an interview with the patient and a perusal of the case notes. Tardive dyskinesia was diagnosed using the research diagnostic criteria of Schooler & Kane (1982), and severity was assessed using the Abnormal Involuntary Movement Scale (AIMS; Guy, 1976).

The following information was recorded from the patient's records: age, length of illness, number of psychiatric admissions, and drug history.

Results

The overall prevalence of TD was 22.5%, with no significant gender difference. Three of 16 males had developed the disorder, and 6 of 24 females. Prevalence of the disorder increased with age (Table I). Six of 11 patients between 50 and 60 years had significant dyskinesia, while only one patient under 40 years showed evidence of the disorder. The mean AIMS score of the patients with TD was 8.6 (s.d. 2.3).

Patients with and without TD did not differ in terms of duration of illness, but those patients with TD had significantly more psychiatric admissions (Mann–Whitney $U=19.5$, $P\leqslant 0.05$). Seven of the nine TD patients were currently on lithium, while 22 of the 32 patients without TD were on lithium (Table II). The two groups differed significantly in terms of duration of lithium therapy, with TD patients on lithium for considerably greater periods of time (Mann–Whitney $U=26.4$, $P\leqslant 0.05$). Groups did not differ in current serum lithium levels, the duration of neuroleptic therapy, or the current neuroleptic dosage.

TABLE I
Age and prevalence of tardive dyskinesia

Age (years)	*Prevalence*
20–30	0/1
30–40	1/14
40–50	2/14
50–60	6/11

TABLE II
Characteristics of patients with and without tardive dyskinesia (mean ± s.d.)

	Involuntary movements present	*Involuntary movements absent*
Length of illness: years	11.5 ± 4.3	10.8 ± 2.9
Number of psychiatric admissions	13.8 ± 5.5	6.1 ± 3.1*
Duration of neuroleptic therapy: years	8.6 ± 3.8	9.4 ± 5.4
Current neuroleptic dosage: chlorpromazine equivalent; mg/day	250.6 ± 130.8	380 ± 195.8
Duration of lithium therapy: years	9.8 ± 3.7	4.2 ± 2.2*

*$P \leqslant 0.05$.

Discussion

A prevalence of 22.5% TD in bipolar patients would indicate that the disorder is no more common in such patients than it is in schizophrenics. This is in contrast to the findings of Rush *et al* (1982), who found a prevalence of 64% in such patients, and those of Waddington & Youssef (1988), who found a prevalence of 40%. Our low figure may be partly explained by the fact that we excluded patients over 60 years of age, as orofacial dyskinesia even in the absence of neuroleptics is high in this group (Klawans & Barr, 1982). The literature to date tends to include or largely focus on elderly patients, whereas we have focused on younger age groups. Our patients had TD of moderate severity as defined by Gardos *et al* (1987), whose patients with severe TD had a mean total AIMS score of 16.5 (s.d. 4.7). A mean score of 8.6 (s.d. 2.3) in the present study contrasts with the findings of Kane *et al* (1984), who suggest that severe TD is common in bipolar patients.

The clear-cut increase in the prevalence of TD with age is in keeping with previous findings (Kane & Smith, 1982; Waddington *et al*, 1985; Waddington & Youssef, 1988), as is the fact that patients with and without TD do not differ in terms of duration of exposure to neuroleptics or current neuroleptic dosage. It is perhaps surprising that average daily neuroleptic intake is so high in a group of bipolar patients (Table II). We are unable to explain this definitively. The sample is representative of our bipolar affective disorder out-patients, and the relatively high neuroleptic intake may be a reflection of prescribing patterns in the district. The finding that patients with TD tend to have more psychiatric admissions might suggest more virulent forms of affective disorder which are less easily stabilised.

When the pharmacological histories of patients with and without TD are compared, the most obvious difference between the groups is the fact that patients with TD had longer durations of lithium exposure. This may indicate that lithium exposure is one of many variables leading to the genesis of TD in patients with bipolar affective disorder, or alternatively it may indicate that a subgroup of bipolar patients are particularly resistant to treatment and biologically prone to the development of TD. Much of the literature to date would indicate that acute lithium administration transiently improves features of TD (Cole *et al*, 1984). The transient improvement brought about by lithium may simply be due to its potential for augmenting the actions of neuroleptics. The net effect of adding lithium may be the same as increasing the dose of neuroleptic, which has long been noted as producing a temporary improvement (Simpson, 1973). The recommendation by the American Psychiatric Association Task Force on Tardive Dyskinesia (Gardos & Casey, 1984) that, because of the high risk of TD, patients with bipolar affective disorder should not be maintained on long-term neuroleptics but on lithium needs further examination in view of the present findings.

References

AMERICAN PSYCHIATRIC ASSOCIATION (1980) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn). Washington DC: APA.

COLE, J. O., GARDOS, G., RAPKIN, R. M., *et al* (1984) Lithium carbonate in tardive dyskinesia and schizophrenia. In *Tardive Dyskinesia and Affective Disorders* (eds G. Gardos & D. E. Casey), pp. 49–73. Washington DC: American Psychiatric Association.

GARDOS, G. & CASEY, D. E. (eds) (1984) *Tardive Dyskinesia and Affective Disorders*. Washington DC: American Psychiatric Association.

——, COLE, J. O., SALOMON, M., *et al* (1987) Clinical forms of severe tardive dyskinesia. *American Journal of Psychiatry*, **144**, 895–902.

GERLACH, J., THORSEN, K & MUNKVAD, I. (1975) Effect of lithium on neuroleptic-induced tardive dyskinesia compared with placebo in a double-blind crossover trial. *Pharmakopsychiatrie/Neuro-Psychopharmakologie*, **8**, 51–56.

GUY, W. (1976) *ECDEU Assessment Manual for Psychopharmacology*, pp. 534–537. Washington DC: US Public Health Service.

KANE, J., STRUVE, F. A. & WEINHOLD, P. (1980) Strategy for the study of patients at high risk for tardive dyskinesia. *American Journal of Psychiatry*, **137**, 1265–1267.

—— & SMITH, J. M. (1982) Tardive dyskinesia: prevalence and risk factors, 1959 to 1979. *Archives of General Psychiatry*, **39**, 473–481.

——, WOERNER, M., WEINHOLD, P., *et al* (1984) Incidence and severity of tardive dyskinesia in affective illness. In *Tardive Dyskinesia and Affective Disorders* (eds G. Gardos & D. E. Casey), pp. 21–28. Washington DC: American Psychiatric Association.

KLAWANS, H. L. & BARR, A. (1982) Prevalence of spontaneous lingual-facial-buccal dyskinesias in the elderly. *Neurology*, **32**, 558–559.

PRANGE, A. J., WILSON, I. C. & MORRIS, C. E. (1973) Preliminary experience with tryptophan and lithium carbonate in the treatment of tardive dyskinesia. *Psychopharmacology Bulletin*, **9**, 36–37.

REDA, F. A., ESCOBAR, J. L. & SCANLEN, J. M. (1975) Lithium carbonate in the treatment of tardive dyskinesia. *American Journal of Psychiatry*, **132**, 560–562.

RUSH, M., DIAMOND, F. & ALPORT, M. (1982) Depression as a risk factor in tardive dyskinesia. *Biological Psychiatry*, **17**, 387–392.

SCHOOLER, N. R. & KANE, J. M. (1982) Research diagnoses for tardive dyskinesia. *Archives of General Psychiatry*, **39**, 486–487.

SIMPSON, G. M. (1973) Tardive dyskinesia. *British Journal of Psychiatry*, **122**, 618.

SMITH, J. M., OSWALD, W. T., KUCHARSKI, T., *et al* (1978) Tardive dyskinesia: age and sex differences in hospitalized schizophrenics. *Psychopharmacology*, **58**, 207–211.

WADDINGTON, J. L., YOUSSEF, H. A., MOLLOY, A. G., *et al* (1985) Association of intellectual impairment, negative symptoms and ageing with tardive dyskinesia: clinical and animal studies. *Journal of Clinical Psychiatry*, **46**, 29–33.

—— & —— (1986) An unusual cluster of tardive dyskinesia in schizophrenia: association with cognitive dysfunction and negative symptoms. *American Journal of Psychiatry*, **143**, 1162–1165.

—— & —— (1988) Tardive dyskinesia in bipolar affective disorder: ageing, cognitive dysfunction, course of illness and exposure to neuroleptics and lithium. *American Journal of Psychiatry*, **145**, 613–616.

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Physical Illness in Chronic Psychiatric Patients from a Community Psychiatric Unit

The Implications for Daily Practice

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The prevalence and significance of physical diseases, and health-care-seeking behaviour, were examined in a sample of 218 chronic psychiatric patients from an urban community psychiatric unit. Only 14% declined medical screening. Of the respondents, 53% had one or more probable or certain physical diseases warranting further medical attention. The majority of the diseases found were minor and typical of primary care problems. A severe (i.e. life-threatening) disease was present in 7% of respondents. Of the patients, 87% visited their GP at least once a year. The implications are that frequent consultation with primary care specialists and health-care-seeking behaviour should be noted, and included in any evaluation of the medical needs of chronic patients in community psychiatric care.

Half of all patients in psychiatric care suffer from one or more physical illnesses, a quarter of which are thought to have causal relationships with the presenting psychiatric disease. The referring agent or therapist involved is, in the majority of cases, unaware of the coexisting physical illness. This is the alarming conclusion of virtually all researchers in the field (Koranyi, 1979; Hall *et al*, 1980; Hoffman & Koran, 1984; Ananth, 1984), and the data are not limited to acute and chronic psychiatric in-patients. Data for chronic psychiatric patients in community care, the focus of the present paper, are quite similar (Barnes *et al*, 1983; Beresford *et al*, 1985).

If the research data are accurate, the inference is that in daily community psychiatric practice, physical disease poses a formidable problem that is often denied. The implication then is that chronic psychiatric patients in community care are deprived of needed medical care and are prone to undetected and severe physical diseases.

Problems in interpreting previous research data in relation to ambulatory care are discussed and incorporated in the present study. The findings of an investigation into the presence of physical disease, patients' health-care-seeking behaviour, and previously undiagnosed disease in chronic psychiatric patients in community care are also reported. Finally, the clinical implications are discussed.

Physical disease and research

The problem of defining physical disease

Physical disease is a concept that is hard to define and often open to interpretation. To quote Dubos, "The difficulty in defining is implicit in the very structure of the word itself" (Dubos, 1968). This statement refers not only to mental disease but also to medical disease (Clare, 1976). In research it is seldom that a definition of, or some criteria for, physical disease is given. In cases where the effort has been made, a considerably lower percentage of physical disease is reported – on average, 20% less (Eastwood & Trevelyan, 1972; Hoogduin *et al*, 1985). 'Diseases' such as lipoma on the back, undescended testicle, hyperlipidaemia, atrophy of one kidney, hyperostosis frontalis interna etc. (Hall *et al*, 1980; Maricle *et al*, 1987) illustrate the problem of definition. Terms such as 'sickness', 'ailment', 'condition', 'handicap', and 'abnormal finding on further examination' are all used interchangeably and sometimes taken for disease.

In psychiatric patients the majority of diseases often go undiagnosed. The label 'misdiagnosis', however, may not be applicable at all. For example, a general practitioner (GP) could well be aware of a physical disorder but, knowing the course of the disorder, not diagnose a disease (e.g. a serological scar from a previous syphilitic infection), while another therapist, not knowing the previous history, might diagnose a luetic infection on a one-time positive serology. A therapist might also apply another definition of physical disease, or a patient might refuse any physical screening procedure while in community psychiatric care. In the available literature, these possibilities are not accounted for but are rather regarded as misdiagnosis. Unfortunately, not all clues can be fully interpreted following a once-only check-up. High blood pressure, for instance, with otherwise no abnormalities detected during the examination, does not justify a diagnosis of uncomplicated hypertension. A follow-up is needed to confirm or exclude the suspected diagnosis. Whether further medical treatment is necessary very much depends on the diagnosis of the severity of the disease. However, only Eastwood & Trevelyan (1972) and Kreitman *et al* (1966) give a severity rating; an indication of certainty of diagnosis is never given.

Community psychiatry and medical care

Community psychiatric care for the chronic patient does not, in general, provide for an evaluation of physical health. Many community psychiatric centres do not include basic facilities and medical manpower for carrying out a routine physical check-up. This was also the case with the unit referred to in the present study. Community psychiatry often operates with multidisciplinary teams. Within the team, individual members tend to assume more responsibility for direct care and management of patients than do their hospital counterparts. The responsibilities of community psychiatric nurses, psychologists, and social workers within the team in the management of physical complaints and symptoms of their patients is not well defined (Davidson *et al*, 1988).

As distinct from in-patient psychiatry, there is, in community psychiatry, a certain overlap with other directly accessible health care services, such as general practice. Clear responsibility for monitoring the physical health of chronic psychiatric patients cannot be shouldered by any ambulatory service and is, in general, left to the better judgement of the patients themselves. Whether chronic psychiatric patients in community care actually use the ambulatory medical resources available to them has not been determined. Adequate utilisation of available resources can, however, be important for their physical well-being.

Chronic psychiatry patients in the community

Stigmatising remarks that are often made regarding chronic psychiatric patients are seldom systematically investigated and are sometimes given as an excuse for deciding against physical screening. Reasons mentioned in the literature include: deteriorated cognitive function, psychological regression, and affective deterioration (Ramsay *et al*, 1982*a*; Ramsay & Engelsman, 1983); prolonged psychiatric history (Ramsay *et al*, 1982*b*); and the adverse impression that chronic psychiatric patients tend to make on others, such as 'malodorous', 'dirty', 'may not co-operate' (Kampmeier, 1977; Hoffmann & Koran, 1984), and 'unattractive and poor' (Adler, 1972). In a recent study (Maricle *et al*, 1987), 43 out of 100 chronic psychiatric patients in community care did indeed decline a medical screening. The above presumptions need to be investigated further so that services can be adapted to patients' traits and handicaps.

Method

In view of the above-mentioned problem of definition traits inherent in community psychiatry, and possible traits in patients, a research project was set up to measure the prevalence both of well-defined physical disease and of functional illness. For research purposes, physical disease was defined as manifestations for which a patient needed medical treatment and/or further medical investigation. Each physical disease was rated according to severity, certainty of diagnosis, and duration of disease. A physical disease which was regarded as being liable to threaten or shorten life was placed in the category 'severe' and all the others were placed in the category 'not severe'. Similar classifications have been used by Eastwood & Trevelyan (1972) and Kreitman *et al* (1966). Given these definitions, the patient, community psychiatric unit (CPU) therapist, GP, and screening specialist in internal medicine were asked for their opinions on the presence of the disease. The use made of medical and mental health care was also measured.

The screening specialist in internal medicine rated all patients on a five-point scale for communicativeness during the interview, memory regarding medical and psychiatric history, physical hygiene, and co-operation during the screening procedures. The data were then compared with those for a matched sample of patients, newly admitted to the internal medicine out-patient clinic of an urban teaching hospital serving the same population.

All patients ($n = 218$) who, at the time of the study, had been receiving treatment for at least one year in an urban community mental health service CPU for chronic psychiatric patients in Maastricht, the Netherlands, were asked to participate in the study. After giving informed consent, each participating patient received an evaluation including an examination by the specialist in internal medicine. The evaluation consisted of a brief, oral general medical history, focusing on past and current symptoms, plus a standardised physical examination as proposed by Summers *et al* (1981). Laboratory studies, including a 20-item automated chemistry panel (SMA-20), a complete blood count (CBC) with differential, an erythrocyte sedimentation rate, a serological test for syphilis (TPHA), thyroid stimulating hormone level (TSH), serum-free thyroxine, urine analysis, and an electrocardiogram (ECG) were obtained for each patient. In addition, the CPU therapist was asked to supply both a medical diagnosis and a diagnosis according to DSM–III (American Psychiatric Association, 1980), grouped in nine main categories, for all patients.

Results

Demographics

Of the 218 patients, 156 (72%) participated in the evaluation; in the other cases, the patient or the therapist or both actively or passively declined the medical evaluation over the 12-month study period. The average age of the participants was 45.5 years (range = 23–62 years; mode = 42 years). The group consisted of 56 men (36%) and 100 women (64%). The majority of men (43%) were unmarried; 41% were married. Of the women 45% were married; 30% were divorced. Most participants were currently living with their family or partner (44%); 30% lived alone. Only 8% were currently employed.

Psychiatric diagnosis, morbidity and treatment

A psychotic disorder was diagnosed in 48 patients, and an affective disorder in 50. Anxiety disorders were exhibited in 24 patients and personality disorders in 53. Substance abuse disorders were found in 7 patients, organic mental disorders in 4, and 12 had some other DSM-III diagnosis. In six patients no certain diagnosis could be agreed upon. There were 33 patients with borderline intellectual functioning (IQ = 74–84).

The average duration of the treatment to date was 4 years (range = 1–31 years). The number of lifetime psychiatric admissions to hospital, as documented in the medical record or specifically identified by the patient, was 1.7; the range was 0–33. The number of admissions to a medical ward during the research year was 15. Patients admitted to a psychiatric ward once or more during the research year numbered 16. Patients currently being treated with psychotropic medication numbered 89 (57%); 32 (20.5%) patients received some type of antipsychotic medication, 22 an antidepressant, 14 a lithium preparation, and 46 received anxiolytic medication on a regular basis.

Frequency of visits to a CPU therapist and GP

In the year preceding the medical examination, the CPU therapists reported an average of 18 visits by their male patients (range = 3–39; median = 3) and 25 by their female patients (range = 3–204; median = 4). GPs were contacted, on average, 4.5 times yearly by the male patients and 6.6 times yearly by the female patients. Of the male patients 16%, and of the female patients 13%, did not attend the GP surgery at all during the research year. Nationwide, the frequency of visits to their GP for males is 2.9 and for females 4.1 per year (Swinkels, 1988).

Previous medical history

A medical condition that was known to be present prior to the study and was being treated either by their GP or a medical specialist was reported by 43 patients (28%). According to the CPU therapist, 51 patients (33%) were known to have a physical disease. In 49 patients (31%) the GP diagnosed a physical disease. Table I delineates the range of conditions.

Use of prescribed medication for non-psychiatric purposes was reported by 32 patients (20.5%); 24 (15%) used prescribed medication for both medical and psychiatric purposes. For 65 patients (42%) only psychotropic medication was prescribed.

Current CPU treatment

The mean length of current treatment was 4 years (range = 1–31 years). Treatment lasted 3–4 years for 58 patients (37%) and 5–6 years for 35 patients (22%). Of the participants, 43% were being treated at the time by a medically trained therapist (i.e. consultant psychiatrist, registrar in psychiatry, or community psychiatric nurse), signifying that over half of the population was not seeing a medically trained therapist on a regular basis.

Physical complaints

At least one physical complaint was described by 137 patients (88%) on a self-report questionnaire which the patients completed before their medical examination. According to the CPU therapist, 130 patients (83%) described one or more physical complaints at the time of the examination. The GP noted one or more physical complaints in 120 (77%) of the patients during their last visit in the research year. When questioned by the specialist in internal medicine, 137 patients (83%) described one or more physical complaints. The number increased to 149 patients (96%) during history-taking (Table II).

Physical examination and laboratory findings

The findings during physical examination provided new information on over half the patients (Table III). On 27 occasions, physical examination resulted in a diagnosis of physical disease. In four cases, suspicion of physical disease during history-taking was rejected following physical examination. The figures indicate the clinical medical importance of routine physical examination.

Abnormalities that showed up in laboratory tests and were judged by the specialist in internal medicine as aspecific and not warranting further evaluation were present in 108 patients (69%). From laboratory tests a diagnosis was established on 28 occasions. As a result of information from laboratory tests on one patient, a previous diagnosis of suspected disease was rejected.

Physical disease

Physical disease of some kind was reported by 43 patients; according to the CPU therapist and GP, the number of patients with one or more physical diseases was 51 (33%) and 49 (31%), respectively (Table II). Physical diseases were diagnosed by the examination, and a fixed set of laboratory studies on each patient. The specialist in internal medicine diagnosed physical disease in 82 patients (53%); on all diagnoses, complete agreement was reached by the specialist and the CPU psychiatrist managing the

TABLE I
Frequency of physical diseases using the International Classification of Primary Care (Wood & Lambert, 1987)

Physical disease therapist	*Patient*	*CPU internal medicine*	*GP*	*Specialist in*
General and unspecific	2	3	2	10
Infectious diseases	1	0	0	1
Multiple trauma	0	1	0	1
Adverse effect of medical agent, proper use	0	1	1	8
Other	1	1	1	0
Blood, blood-forming organs, lymphatics, spleen	1	1	1	0
Digestive system diseases	5	7	6	15
Eye and ear diseases	1	2	5	2
Circulatory system diseases	12	17	17	32
Uncomplicated hypertension	6	7	8	15
Hypertension with secondary complications	1	0	2	2
Other	5	10	7	15
Musculoskeletal diseases	11	5	9	13
Osteoarthritis of spine	4	0	2	0
Back pain with radiating symptoms	1	1	1	5
Rheumatoid arthritis and allied conditions	3	2	1	0
Other	3	2	6	8
Neurological diseases	5	6	3	6
Migraine	3	3	0	0
Other	2	3	3	6
Respiratory diseases	7	5	8	7
Chronic bronchitis/bronchiectasis	6	5	7	7
Other	1	0	1	0
Skin diseases	1	6	6	3
Endocrine, metabolic and nutritional diseases	8	8	9	15
Morbid obesity	0	1	2	3
Diabetes mellitus	4	2	3	6
Hyperthyroidism	2	1	1	1
Other	2	4	3	5
Urinary system diseases	4	5	3	6
Syphilis male/female	0	1	2	2
Other diseases	1	0	1	1

research (A. Honig). Table IV delineates the 67 newly diagnosed physical diseases.

The specialist in internal medicine diagnosed, in all, 112 physical diseases. Circulatory diseases were most frequently found, followed by endocrine and metabolic diseases (Table I). For 53 (47%) of the diseases, an approximate duration could be given. Nine diseases (17%) lasted less than 1 year, 10 (18.9%) lasted between 1 and 3 years, and 34 (64.1%) lasted longer than 3 years. Applying the earlier definition of severity, the specialist in internal medicine rated 13 physical diseases in 11 patients (7%) as severe and 87 as not severe. For eight diseases, no definite conclusion could be given of the severity. A rating of certainty present was given for 56 diseases (50%). Thirteen diseases were

TABLE II
Physical complaints and diseases

	Patient	*CPU therapist*	*GP*	*Specialist in internal medicine*
Physical complaint	88%	83%	77%	83%
(one or more per patient)	$n=137$	$n=130$	$n=120$	$n=129$
Physical disease	28%	33%	31%	53%
(one or more per patient)	$n=43$	$n=51$	$n=49$	$n=82$
Severe physical disease		6%	4%	7%
(one or more per patient)		$n=9$	$n=6$	$n=11$

TABLE III
Physical examination (PE) findings

Finding	Number
Elevated blood pressure	14
Weight 10% high limit	20
Low limit	4
Any PE abnormal finding (excluding neurological)	56
Any neurological finding	8
No confirmation of abnormality as suspected following history-taking	4
No abnormal finding	73

rated as being both severe and certainly present; seven of these were circulatory diseases, three were endocrine and three were other diseases. Of the 67 newly diagnosed physical diseases, only three were rated as severe; in five cases, no indication of severity could be given. Of the newly diagnosed diseases, 25 were rated as being certainly present.

Agreement on the presence of a physical disease

In 55 patients (35%), all four participants agreed on the absence of one or more defined physical diseases. In the other patients (65%), at least one of the participants described one or more physical diseases. The factual agreement on the presence or absence of one or more defined physical diseases per patient between the specialist in internal medicine and the CPU therapist, GP, and patient was moderate (Table V), with Cohen's kappa not exceeding 0.35. On the presence or absence of one or more severe, certainly present physical diseases, as diagnosed by the specialist in internal medicine, agreement with the GP and CPU therapist was even less (Table VI). For clinical reasons, no ratings of severity were asked of the patient himself.

TABLE IV
Newly diagnosed physical diseases

Disease	*Number of cases*
Adverse effect of medical agent, proper use	6
Infectious disease	1
Hiates (diaph.) hernia	3
Cirrhosis/other liver disease	4
Other disease, digestive system	4
Diseases of the eye	1
Chronic ischaemic heart disease	3
Chronic bronchitis	1
Atopic dermatitis	1
Uncomplicated hypertension	2
Other diseases, circulatory system	3
Morbid obesity	2
Diabetes mellitus	3
Other endocrinological, metabolic and nutritional diseases	3
Back pain with radiating symptoms	3
Traumatic arthritis/arthropathy	2
Other disease, musculoskeletal system	4
Disease of neurological system	4
Elevated blood pressure	4
Cystitis/other urinary infections	4
Infections, non-veneral	4
Uterovaginal prolapse	1
Other disease, urinary system	4

TABLE V
Agreement on the presence of one or more diseases per patient

Specialist in internal medicine	*Disease*	*No disease*	*Total number*
GP[1]			
Disease	40	42	82
No disease	9	65	74
Total number	49	107	156
CPU[1]			
Disease	41	41	82
No disease	10	64	74
Total number	51	105	156
Patient[2]			
Disease	36	46	82
No disease	7	67	74
Total number	43	113	156

1. $\kappa=0.35$.
2. $\kappa=0.33$.

Of the 13 severe and certainly present physical diseases, diagnosed by the specialist in internal medicine, nine (70%) were known to both the GP and CPU, although they were not always rated as being severe and certainly present.

Functional illness

Physical complaints for which no organic abnormal functioning could be detected were rated as aspecific; of the three main physical complaints, one or more aspecific physical complaints were present in 136 patients (87%). The specialist in internal medicine diagnosed 114 patients (73%) as having one or more functional illnesses, ranging from irritable bowel syndrome to tension headache. By comparison, in only 47 patients (20%) were physical complaints present for which an organic cause could be detected.

TABLE VI
Agreement on the presence of one or more severe and certain diseases per patient

Specialist in internal medicine	*S+C disease*	*No S+C disease*	*Total number*
GP[1]			
S+C disease	3	8	11
No S+C disease	3	142	145
Total number	6	150	156
CPU[2]			
S+C disease	3	8	11
No S+C disease	6	139	145
Total number	9	147	156

1. $\kappa=0.29$.
2. $\kappa=0.22$.

Non-respondents

Patients not participating in the project numbered 62 (28%). Of the whole research population, only 30 patients (14%) declined medical evaluation. For half the group of non-respondents, the CPU therapist advised against evaluation for one reason or another. In 13 cases, there was either no contact with the patient or the patient could not be traced (no fixed residence). The CPU therapist collected the same demographic and diagnostic data from both the respondents and the non-respondents. There were no statistical differences in demographic data. For diagnosis according to the DSM-III, personality disorder, substance abuse, and psycho-organic disorders were over-represented in the non-respondent group. The CPU therapist noted considerably fewer physical complaints in the non-respondent group: 52% compared with 82% in the respondent group. The number of physical diseases was equal in both groups.

Patients' behaviour

In the present study only 31 patients (14%) refused to co-operate in the project. The ratings on a five-point scale by the specialist in internal medicine on communicativeness, ability to recall medical and psychiatric history, physical hygiene, degree and quality of activity, co-operation and global impression were compared with those of 60 matched, new patients attending an internal medicine out-patient clinic. The ratings for all these items shows no significant differences.

Discussion

Somatic complaints and symptoms were almost invariably present in this sample of chronic psychiatric patients in community care. Almost three-quarters of the patients were diagnosed as having a functional disorder; nearly half the patients were medically ill, but hardly any severe physical diseases were found. The bulk of the physical diseases that were detected could easily be dealt with by the GP.

Although a longer-term follow-up is still in progress, it seems that medical treatment of the diagnosed diseases does not change the chronic psychiatric problems dramatically. Certainly no mimics (i.e. organic conditions erroneously taken for psychiatric diseases) were found. Our data confirm Maricle *et al*'s findings (1987) in a similar setting with a smaller and diagnostically less diverse sample of chronic community psychiatric patients than ours. It seems safe to say that, at least in our local health care system, no medical attention is withheld from our sample of chronic psychiatric patients in community care. More specifically, our group of chronic psychiatric patients in community care is, in general, very capable of making use of available ambulatory health care services. During a physical screening procedure, they do not significantly differ in behaviour from a non-psychiatric ambulatory population, and they are, in the majority of cases, prepared to co-operate in a 2-hour physical screening procedure. There is little agreement on the part of all participants regarding the physical health of this population of patients. This does not, as such, signify a high percentage of misdiagnosing, but could be interpreted as a trait inherent in the interaction between the patient and the specific health care therapist (GP, CPU therapist, or specialist in internal medicine).

Somewhat alarming, however, was the high percentage of newly diagnosed diseases induced by psychotropic medication. More than half the patients (57%) used some prescribed psychotropic medication. Fourteen of these patients were taking lithium carbonate at the time of the study. Of these 14 patients, 6 were diagnosed by the specialist in internal medicine as suffering adverse effects of this medication. Five of these patients were possibly mildly hypothyroid. This was, in all five cases, unknown to the prescribing CPU therapist. Evaluation of laboratory thyroid functioning is, very likely, hampered by the absence of direct access to laboratory facilities in Dutch community psychiatric units.

Perhaps the most important finding to come out of this study is the need for close co-operation between the GP and the CPU therapist. In the first place, there is a need to identify those patients who do not make adequate use of health care services and who are thereby potentially at risk. Secondly, when working together, the GP and CPU therapist can more adequately screen and diagnose severe physical diseases – 70% of the diseases that the specialist in internal medicine rates as being severe and certainly present. The co-operation with the GP could well be carried out by a CPU therapist of any discipline. The consultation could result in a referral to a CPU psychiatrist or to a GP for further evaluation. Whenever physical screening is carried out, history-taking and the performance of a routine, standardised physical examination (Summers *et al*, 1981) seem to be the most valuable elements in the entire diagnostic procedure. Somatic fixation or denial, on the part of both CPU therapist and patient, could be prevented by the above recommended physical screening procedures.

References

Adler, T. (1972) Helplessness in the helpers. *British Journal of Psychology*, 45, 315–326.

American Psychiatric Association (1980) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn) (DSM-III). Washington, DC: APA.

Ananth, J. (1984) Physical illness and psychiatric disorders. *Comprehensive Psychiatry*, 25, 586–593.

Barnes, F. B., Mason, J. C., Greer, C., *et al* (1983) Medical illness in chronic psychiatric out-patients. *General Hospital Psychiatry*, 5, 191–195.

Beresford, T. P., Hall, R. C. W., Wilson, F. C., *et al* (1985) Clinical laboratory data in psychiatric out-patients. *Psychosomatics*, 26, 731–744.

Clare, A. (1976) *Psychiatry in Dissent*. London: Travistock Publications.

Davidson, R. E., Factor, R., Grundlack, E., *et al* (1988) Psychiatric nursing roles in a community mental health center. *Community Mental Health Journal*, 24, 83–86.

Dubos, R. (1968) *Man, Medicine and Environment*. London: Pall Mall Press.

Eastwood, M. R. & Trevelyan, M. H. (1972) Relationship between physical and psychiatric disorder. *Psychological Medicine*, 2, 363–372.

Hall, R. C. W., Gardner, E. R., Stickney, S. K., *et al* (1980) Physical illness manifesting as psychiatric disease. *Archives of General Psychiatry*, 37, 989–995.

Hoffman, R. S. & Koran, L. M. (1984) Detecting physical illness in patients with mental disorder, *Psychosomatics*, 25, 654–660.

Hoogduin, C. A. L., Haan, E. de & Terluin, B. (1985) Somatische aandoeningen bij opgenomen psychiatrische patiënten (Somatic illness in psychiatric in-patients). *Tijdschrift voor psychiatrie*, 27, 105–114.

Kampmeier, M. H. (1977) Diagnosis and treatment of physical disease in the mentally ill. *Annals of Internal Medicine*, 86, 637–645.

Koranyi, E. K. (1979) Morbidity and rate of undiagnosed physical illnesses in a psychiatric clinic population. *Archives of General Psychiatry*, 36, 414–419.

Kreitman, N., Pearce, K. I. & Ryle, A. (1966) The relationship of psychiatric, psychosomatic and organic illness in a general practice. *British Journal of Psychiatry*, 112, 569–579.

Maricle, R. A., Hoffman, W. F., Bloom, J. D., *et al* (1987) The prevalence and significance of medical illness among chronically mentally ill out-patients. *Community Mental Health Journal*, 23, 81–90.

Ramsay, R. A., Krakowski, A. J., Rydzynski, Z., *et al* (1982*a*) International comparison of the prevalence of psychosomatic disorders in schizophrenic patients. *Psychotherapy and Psychosomatics*, 38, 206–220.

——, Ananth, J., Engelsmann, F., *et al* (1982*b*) Schizophrenia and psychosomatic illness. *Journal of Psychosomatic Research*, 26, 33–42.

—— & Engelsmann, F. (1983) Epidemiology of psychosomatic disorders in schizophrenic patients: methodological issues. *Psychotherapy and Psychosomatics*, 40, 148–157.

Summers, W. K., Munoz, R. A. & Read, M. R. (1981) The psychiatric physical examination–Part I: Methodology. *Journal of Clinical Psychiatry*, 42, 95–98.

Swinkels, H. (1988) Gezondheidsenqûtes, trendcÿfers gezondheidsenquête 1981–1987 (Health survey 1981–1987). *Maandbericht Gezondheidsstatistiek*, 8, 14–28.

Wood, M. & Lambert, H. (1987) *International Classification of Primary Care*. Oxford: Oxford University Press.

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Benefits and Problems of Routine Laboratory Investigations in Adult Psychiatric Admissions

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A survey of laboratory investigations in the management of 1007 non-geriatric admissions to a district general hospital adult psychiatric unit showed a wide variation in the number of tests performed, and in the abnormal proportion between test types. Despite a policy of screening on admission, 40% of admissions had no tests. Physical illness attributable to mental illness was common, but rarely serious and usually apparent clinically. Mental illness attributable to physical illness detected by laboratory tests was rare: five cases of thyroid disease in women with affective disorder, and two cases of chest infection with raised white cell count in sustained mania. The findings show that tests are frequently used in circumstances where the result is of no apparent value. Test use might be improved by restricting screening to thyroid function and laboratory urine analysis, each in women. There are particular indications for white cell count in sustained or unexplained relapse of mental illness, and for syphilis serology when disinhibition may have exposed the patient to infection.

Mental and physical illness coexist by a number of mechanisms. Firstly, diseases cluster more than would be expected by chance (Hinkle & Wolff, 1957; Eastwood & Trevelyan, 1972). Maguire & Granville-Grossman (1968) showed 17% of 200 psychiatric admissions to have incidental physical morbidity, half of whom required transfer to a medical ward. Secondly, mental illness can have physical effects through abnormal diet or behaviour or the mechanisms of psychoimmunology (*Lancet*, 1987). Thirdly, physical illness or its treatment can have mental effects (Lloyd, 1977; Hall *et al*, 1981). Most studies of medical in-patients show a psychiatric morbidity of around 25% (*Lancet*, 1979). Fourthly, psychotropic drugs have adverse or toxic side-effects, whether used in treatment, abuse, self-harm, or by accident.

These mechanisms influence the way the laboratory is used. Tests may be used on apparently physically well patients for screening, on those with a suspected physical illness for diagnosis, and on those with a known physical illness for management. The number of tests used to investigate a disease can vary 20-fold between hospitals (Ashley *et al*, 1972; Daniels & Schroeder, 1977), and teaching and research can take investigation beyond clinical need (Griner & Glaser, 1982; Reuben, 1984). The act of testing can be therapeutic (Sox *et al*, 1981), and the laboratory may be used to generate income (Schroeder & Showstack, 1978; Moloney & Rogers, 1979). Certain criteria make tests useful: prevalence of disease must be adequate, tests must have appropriate sensitivity and specificity, and benefit must be expected from an abnormal result.

The mentally ill pose special problems. History taking, examination, and practical procedures may be difficult, and psychiatrists may be less familiar with indications and uses of tests and their interpretation. Definitive studies of the relationship of the laboratory to clinical practice exist in general medicine (Hampton *et al*, 1975; Hecker, 1975), surgery (Forrest *et al*, 1981; Kaplan *et al*, 1985), paediatrics (Leonard *et al*, 1975), geriatrics (Hodkinson, 1981), and primary care (Mills & Reilly, 1983; Hartley *et al*, 1984; Forrest *et al*, 1987), but psychiatry has received less attention.

We have examined the management of admissions to our district general hospital adult psychiatric unit. Radiology and thyroid tests are reported separately (White & Barraclough, 1986, 1988). We aim here to establish the pattern and benefits of laboratory use.

Method

The Department of Psychiatry of the Royal South Hants Hospital, Southamptom, provides a service for 200 000 people aged 16–65 years in a catchment area of 300 000. Adult psychiatry accounts for 32% of the beds and 11% of admissions; children under 16 and the elderly are treated elsewhere.

We examined the case notes of psychiatric patients admitted between 1 January 1983 and 30 April 1984, covering about 1000 admissions, and recorded the laboratory results obtained in clinical management. Routine haematology and biochemistry tests are requested by the doctor in charge of the admission at the time of clerking, and further tests are requested after review, usually at the ward round. If the test had been repeated during an admission, the first result was taken. Results falling outside the reference range given by the laboratory were termed abnormal, and the clinical findings documented in the notes at the time were recorded. Clinical findings were termed positive if a pathological finding had been recorded in any part of the medical history or physical examination.

Haematological tests of haemoglobin, mean corpuscular volume, and total white cell count are measured by automated counter, which also computes red cell indices. The laboratory reference range is taken from a standard text, Dacie & Lewis (1975), which itself takes a consensus of several surveys. Erythrocyte sedimentation rate was not recorded, as the reference range is unclear, and the test is not useful for screening (Sox & Liang, 1986). Chemical pathology is performed on 6-channel and 13-channel autoanalysers. The number and type of tests performed by these machines may vary from day to day. Other tests are undertaken singly. The reference ranges are those used by the laboratory for healthy adults. Psychiatric diagnoses were taken from the Southampton psychiatric case register.

Results

Demography

The 1007 admissions were accounted for by 719 patients, 182 having one or more readmissions during the period. Compared with the catchment population, the admissions comprised more men over and fewer under 25, and more women over and fewer under 35. Only 19 admissions were aged 65 or over (Table I).

Investigation rates

The 1843 requests produced 8663 results, the difference attributable to the use of autoanalysers. Forty per cent of admissions had no results, a rate similar to that in other admission screening programmes in psychiatry (Bannister *et al*, 1987). A further 40% had one haematology and one biochemistry automated analysis each, accounting for 90% of all results; the remaining 20% had single investigations alone or in addition.

A mean of 14 results were obtained from each of the 60% of admissions investigated, a rate similar to that in Whitehead & Wootton's (1974) study in general medicine.

The rate of investigation was related to diagnosis ($\chi^2 = 24.5$, d.f. = 6, $P < 0.001$); the diagnoses with most and least investigations, affective and personality disorder respectively, contributed most of the variance. When these two diagnoses were eliminated from the calculation, the difference between the remaining diagnoses was not significant.

Investigation varied little with age until increasing for patients aged over 55 years (Table I).

Abnormality rates

Of the 8663 results, 887 (10.2%) were reported to be abnormal. Of the 610 admissions tested, 374 (61%) had at least one abnormal result. The modal number of abnormal results was two, which is expected with multiple tests, even in the healthy (Sackett, 1973). The percentage abnormal was associated with diagnosis ($\chi^2 = 44.8$, d.f. = 6 $P < 0.001$); the diagnoses with most and least percentage abnormal, alcoholism and schizophrenia respectively, contributed most. When these two diagnoses were eliminated from the calculation, the difference was not significant. The percentage abnormal varied little with age, until increasing for patients aged over 65 years (Table I). Our rate of 10.2% of tests giving abnormal results is lower than that in other studies in psychiatry – Thomas (1979) found 13% of 2895 results abnormal, and Ferguson & Dudleston (1986) 17% of 2753 abnormal. Positive clinical findings accompanied fewest abnormal test results in the 25–34-year-olds and most in the 55–64-year-olds (Table I).

Important results

Described below are the tests that yielded the 73 abnormal results making important contributions to diagnosis or management (compare with Table II).

Thyroid function tests

The 300 thyroid function tests were accounted for by 259 patients. Ten results were abnormal, accounted for by

TABLE I

Age and sex distribution of admissions, and test results

Age: years	*Population*		*Admissions*			*No. of tests*			
	% male	*% female*	*% male (n)*	*% female (n)*	*% having any test (n)*	*Total*	*Average per admission*	*Abnormal results (n)*	*Clinical findings positive (% of abnormal results)*
15–24	25	24	11 (58)	13 (66)	62 (76)	957	7.7	7 (67)	46
25–34	24	23	26 (128)	16 (81)	53 (109)	1525	7.3	9 (135)	42
35–44	18	19	28 (137)	23 (116)	53 (133)	1835	7.2	11 (209)	56
45–54	16	18	22 (113)	22 (110)	64 (42)	2147	9.6	10 (221)	61
55–64	16	18	13 (68)	22 (111)	75 (133)	1941	10.8	11 (218)	64
>65			2 (8)	3 (11)	79 (15)	258	13.6	14 (37)	63

TABLE II

Test	*Total no. of tests*	*No. abnormally*		*Total no. abnormal n (%)*	*Clinical findings positive (% of abnormal results)*
		low (%)	*high (%)*		
Haematology					
Haemoglobin[1]	504	20 (4)	1 (0)	21 (4)	45
Mean corpuscular volume[1]	503	10 (2)	40 (8)	50 (8)	66
White cell count[1]	504	5 (1)	72 (14)	77 (15)	58
Blood film	40	– –	– –	18 (45)	67
Vitamin B_{12}	22	1 (5)	– –	1 (5)	0
Folate	20	1 (5)	– –	1 (5)	0
Chemical pathology					
Sodium[1]	517	17 (3)	6 (1)	23 (5)	65
Potassium[1]	514	44 (9)	7 (1)	51 (10)	69
Chloride[1]	481	17 (4)	35 (7)	52 (11)	37
Bicarbonate[1]	507	115 (23)	6 (1)	121 (24)	44
Creatinine[1]	517	– –	15 (3)	15 (3)	80
Urea[1]	523	– –	91 (17)	91 (17)	41
Calcium total[1]	462	10 (2)	36 (8)	46 (10)	47
adjusted	462	7 (2)	5 (1)	12 (3)	23
Inorganic phosphate[1]	444	69 (16)	0 –	69 (16)	42
Total protein[1]	457	5 (1)	35 (8)	40 (9)	45
Albumin[1]	455	1	5 (1)	6 (1)	67
Bilirubin[1]	465	– –	34 (7)	34 (7)	59
Alkaline phosphatase[1]	462	– –	31 (7)	31 (7)	81
Aspartate transaminase[1]	454	– –	66 (15)	66 (15)	77
Glutamyl transpeptidase	54	– –	22 (41)	22 (41)	91
Glucose	136	0 –	13 (10)	13 (10)	77
Syphilis serology	136	– –	– –	5 (4)	60
Thyroid function tests	300	5 (2)	5 (2)	10 (3)	80
Autoimmune screen	24	– –	– –	9 (38)	100
Porphyrins	6	– –	– –	0 –	0

1. Components of autoanalysers.

nine patients. Two of the nine settled spontaneously, and were probably due to the euthyroid sick syndrome, a transient abnormality of thyroid hormone during non-thyroid illness, which seems to be under-recognised (Gooch *et al*, 1982). Five of the nine were known cases, and the remaining two were new diagnoses. All seven cases were women with an affective disorder, four of whom had a past history and two of whom had a family history of thyroid disease. No patients giving abnormal results were taking lithium. Thyroid disease was thought to have precipitated the mental illness in five patients, including the two newly diagnosed with thyroid disorder. They are described elsewhere (White & Barraclough, 1988).

Syphilis serology

One patient with active and one with treated syphilis acquired their infection while disinhibited through mental illness. Three other patients had positive results from treated infection. Psychiatric patients appear at risk of infection because of their mental illness, rather than vice versa. Selective screening of those exposed to risk is indicated (Hart, 1986).

Urinalysis in women

Of 97 biochemical and bacteriological tests of urine in women and 59 in men, 15 in women showed infection. Five of the 15 were asymptomatic, their infection detected only by screening.

White cell count

Seventy were raised and five were low. Many raised results were accounted for by smoking (Howell, 1970) or lithium treatment (Murphy *et al*, 1971). Underlying pathology may also be unmasked; 12 raised counts were associated with chest infection, of which two had intractable mania which only resolved when the chest infection was treated. Selective screening may be warranted when clinical signs are present or the psychiatric illness becomes protracted.

Glucose

The 13 abnormal results included three new diagnoses of diabetes of mature onset; each was suspected from clinical findings, and the test was necessary for diagnosis. In ten known cases the test was necessary for management.

Mean corpuscular volume

Fifty results were abnormal, 10 microcytic, and 40 macrocytic. Forty-eight of the 50 were suspected from alcohol abuse or other clinical findings, or from low levels of haemoglobin. The remaining two were not clinically important.

Blood film examination

All 18 abnormal patients had positive clinical findings (12 cases), abnormal blood count (13), or both (7). Screening appears unnecessary, but the usual medical indications are shown to be worthwhile (Hamblin, 1983).

Liver function tests

Of 1435 liver function tests, 153 were abnormal; 117 were associated with positive clinical findings, in 79 with alcohol abuse. As almost all newly admitted patients receive psychotropic drugs, the abnormal results can be attributed to alcohol, and can be expected. Only raised aspartate transaminase levels were significantly associated with alcoholism ($\chi^2=71$, d.f. = 6, $P<0.001$). All bilirubin and alkaline phosphatase estimations repeated at follow-up were normal, except for one patient newly diagnosed with Gilbert's syndrome. Of 41 repeated aspartate transaminase tests, 12 of the 16 patients who remained abnormal were known to have continued to abuse alcohol.

In summary, clinical findings are so regularly present that use of liver function tests for screening or diagnosis of alcoholism is unwarranted. The laboratory may occasionally help management (Latchman, 1986; Skinner *et al*, 1986).

Potassium

Forty-four results were low and seven raised. There was an unexplained association between a low result and a psychiatric diagnosis of personality disorder ($\chi^2=14.4$, d.f. = 6, $P<0.001$). Low results may arise in the specimen stored warm, when potassium passes into red cells with glucose, or in the patient with chronic hyperventilation causing a respiratory alkalosis and kaliuresis. Screening is not necessary as most abnormal results are not clinically important.

Bicarbonate

One hundred and fifteen were low and six raised. Low results may arise from respiratory alkalosis in the chronic hyperventilation syndrome or from ketosis of starvation. Screening is not necessary as most abnormal results are not clinically important.

Urea

Ninety-one were raised, with a significant association with a psychiatric diagnosis of organic disorder ($\chi^2=12.7$, d.f. = 6, $P<0.001$). Mental illness, particularly organic psychosis, may contribute through dehydration. Only seven patients also had raised creatinine levels. No renal failure or unsuspected pathology was detected. Screening is unnecessary.

Phosphate

Sixty-nine were low. Hypophosphataemia may arise from menstruation, drugs such as barbiturates, antacids or oral contraceptives, or eating after starvation (Ritz, 1982; Cumming *et al*, 1987). Screening is unnecessary, but the test is indicated when sudden resumption of eating accompanies psychiatric treatment.

Discussion

The role of tests

A test has a screening role when an abnormal result is not expected, and a diagnostic or management role when the result is expected from clinical findings. Ideally, tests of high sensitivity are used for screening, and of high specificity for diagnosis. Sensitivity and specificity can be varied by having a choice of reference ranges which allow the same test to be used for different roles.

Criteria for abnormality

Reference ranges are conventionally two standard deviations either side of the mean, covering 95% of results, as most variables have a normal or log-normal distribution which enables use of parametric statistics. Many of the remaining 5% fall just outside the reference range and are false positives which are abnormal only statistically (Fig. 1).

Problems arise because of rigid interpretation of the reference range by clinicians who are remote from the laboratory sciences. A result tends to be noted as abnormal irrespective of its magnitude, context, and meaning, and further investigation is instigated. A wider reference range, say three standard deviations, would encompass 99.7% of values and reduce the number of false positives. The use of alternative reference ranges or 'action limits' would involve the clinician in selecting the appropriate cut-off for his particular situation. However, action limits have disadvantages; for example, the laboratory must know the distribution of results more precisely, and true positives may be missed.

A choice of reference range is not routinely available, and results are interpreted here as they are in practice, as normal or abnormal. Not all abnormal results are important, as 5% of these are to be expected; in addition, many results have a bias to their distribution that invalidates the reference range supplied, as Fig. 1 demonstrates. Tests can be considered according to whether the abnormal exceed this expected 5%.

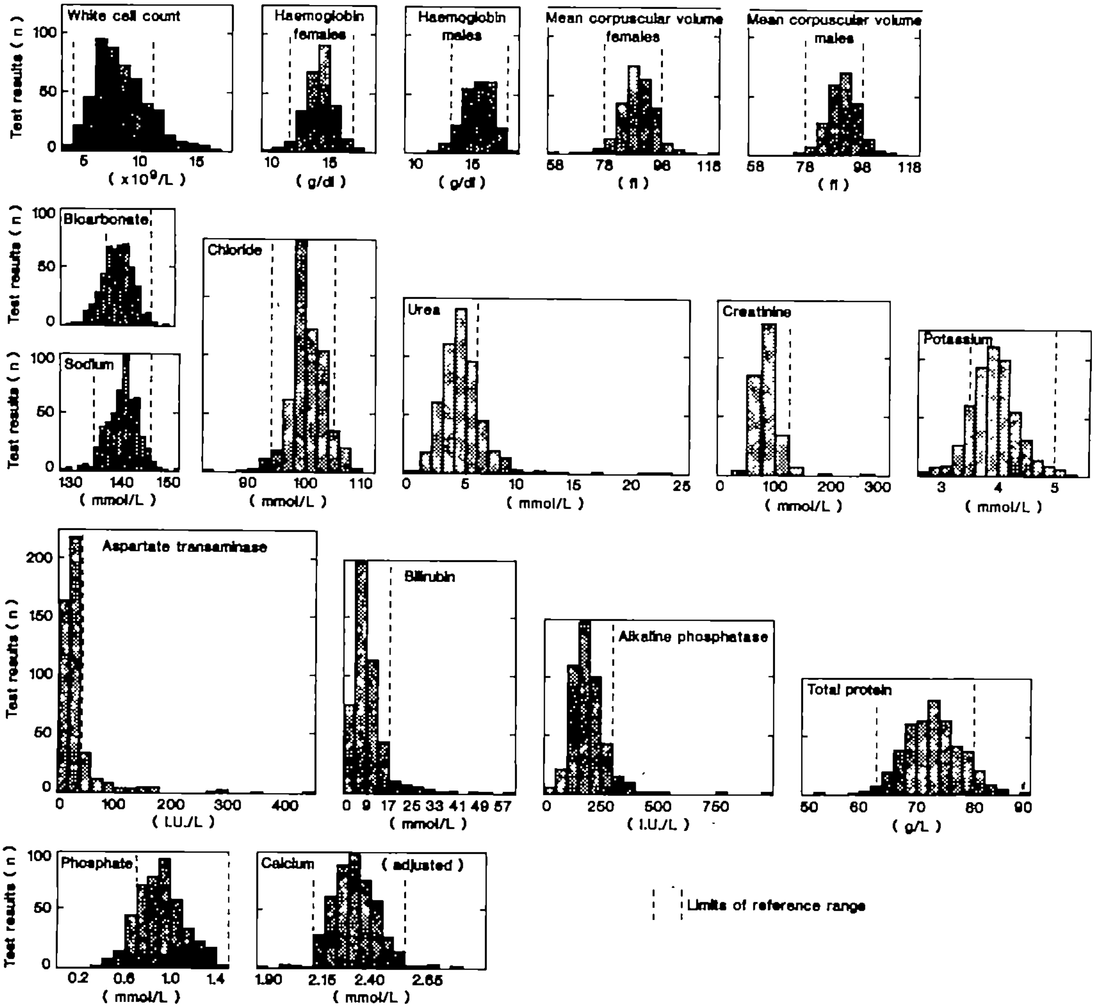

FIG. 1 Distribution of results for individual tests.

(a) Tests with only the expected rate abnormal. Tests with less than 5% abnormal may be necessary for management, as with creatinine in lithium treatment, or for diagnosis, as with thyroid function and syphilis serology. Tests are unnecessary where no important pathology or cause of mental illness is detected, as here with haemoglobin, vitamin B_{12}, folate, sodium, calcium, and porphyrins.

(b) Tests with anticipated increase in percentage abnormal. Some results are necessary for diagnosis or management even when expected from clinical findings, as with glucose or autoantibodies. Others are so predictably abnormal that they are unnecessary, as with mean corpuscular volume, blood film, or liver function tests.

(c) Tests with unanticipated increase in percentage abnormal. Where the excess beyond 5% is not expected from clinical findings, the role of the test continues to be screening. A few results have clinical importance, as with urinalysis for women. In most cases the excess is likely to be due to spurious effects on the distribution of results in psychiatric patients, as with protein, potassium, chloride, bicarbonate, urea, and phosphate (Fig. 1).

Sources of error

Psychiatric patients may differ from other populations in effects of diagnosis, age, sex, season, activity, posture, diet, and use of drugs and alcohol. A fundamental factor such as mobility may influence levels of plasma proteins and protein-bound anions as psychiatric patients, who are not bed bound, have higher levels (Fig. 1).

Individual patients may have results influenced by hyperventilation, pregnancy, or menstruation. Individual specimens may be influenced by haemostasis during sampling, by delay, contamination, agitation or temperature during transport, or analytical errors. Therefore excess abnormal results may be either truly pathological or false positive artefacts.

Relationship between physical and mental illness

Mental illness causing physical illness accounts for many abnormal results. Deliberate self-harm, usually overdose, can require medical treatment. Abuse of drugs or alcohol influences mean corpuscular volume and liver function. Dietary neglect disturbs fluid and electrolytes. Bizarre or disinhibited behaviour can lead to any abnormality; two patients contracted syphilis. Transiently abnormal results related to disturbed behaviour and emotions are also seen, here with thyroid function in two patients and with glucose in another.

Physical illness causing mental illness is rare but important. In five cases thyroid disease appeared to cause mental illness. Chest infection apparently perpetuated two cases of mania and possibly ten other episodes of mental illness. Other studies vary widely; Willett & King (1977) found no physical cause in 636 admissions, Herridge (1970) found 21% in 209 admissions, and Hall *et al* (1978) 49% in 100 severely ill compulsory admissions in the USA.

Mental and physical illness may be unrelated, either as false positives or as incidental morbidity.

Costs

Good practice involves the correct level of investigation; too much is bad, as well as too little, as resources are diverted away from other needs, known in health economics as 'opportunity cost' (Fleming & Zilva, 1981; Mooney & Drummond, 1982; Thurow, 1985). What has been the actual cost of detecting the 73 clinically important findings here? Available methods of costing remain very artificial, and the cost is apparently small. Relying chiefly on Tarbit's (1986) methods gives £7499.33 for the 8663 investigations.

Reservations should be borne in mind about this figure. Firstly, Tarbit notes some indirect costs are not included. Secondly, testing may affect management in ways that elude measurement, such as prolonging hospital stay. Thirdly, testing has various non-financial disadvantages: unsolicited results pose problems of confidentiality and ethics (Knight, 1986). If some are false positives, the problems are compounded (Bradwell *et al*, 1974).

Benefits

Tests give benefits other than the detection of disease. Patients may be reassured by investigation (Sox *et al*, 1981), and doctors may feel more confident with investigations rather than a history and examination, particularly if severe mental illness impairs co-operation, although this will depend on the experience and skills of the individual. Results may also have a role in clinical teaching.

Further inquiries

The opposing pressures of budgetary restraint on the one hand, and litigation on the other, may require justification of practice by clinical audit. The effectiveness of audit has been established in medicine (Cohen *et al*, 1982; Everett *et al*, 1983; Fowkes, 1985; Fowkes *et al*, 1986) but not in psychiatry.

This study makes the initial step of an audit of current practice, but a prospective survey is desirable. In psychiatry the distribution of results and reference

TABLE III
Recommendations for routine use of the laboratory in in-patient adult psychiatry

Test	*Indications*	*Comment*
Thyroid function tests	Women with affective disorder. Past or family history of thyroid disease	In all cases delay testing until or repeat in the third week after admission to avoid transitory rise of euthyroid sick syndrome
Laboratory 'urinalysis'	Women	Even when asymptomatic
White cell count	Unexplained unremitting episode of psychiatric illness	
Syphilis serology	Exposure to risk of infection	
Other investigations		Use for medical diagnosis or management as opposed to screening

ranges may be unique, and could be established by testing every patient admitted, a recognised research strategy (Hecker, 1975; Hampton, 1983; Reuben, 1984).

Conclusions

This survey does not support the extent of investigation commonly seen in adult psychiatry: the findings justify only those tests in Table III. Others may be indicated when physical treatments require management. Use of these guidelines would eliminate expense and risk without sacrificing detection.

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References

Ashley, J. S. A., Pasker, P. & Beresford, J. C. (1972) How much clinical investigation? *Lancet*, *i*, 890–892.

Bannister, P., Mortimer, A., Shapiro, L., *et al* (1987) Thyroid function screening of psychiatric inpatient admissions: a worthwhile procedure? *Journal of the Royal Society of Medicine*, **80**, 77–78.

Bradwell, A. R., Carmalt, M. H. B. & Whitehead, T. D. (1974) Explaining the unexpected abnormal results of biochemical profile investigation. *Lancet*, *ii*, 1071–1074.

Cohen, D. I., Jones, B. & Neuhauser, D. (1982) Does cost information availability reduce physician test usage? *Medical Care*, **20**, 286–292.

Cumming, A. D., Farquhar, J. R. & Boucher, I. A. D. (1987) Refeeding hypophosphataemia in anorexia nervosa and alcoholism. *British Medical Journal*, **295**, 490–491.

Dacie, J. V. & Lewis, S. M. (1975) *Practical Haematology* (5th edn). Edinburgh: Churchill Livingstone.

Daniels, M. & Schroeder, S. A. (1977) Variation among physicians in use of laboratory tests. *Medical Care*, **15**, 482–487.

Eastwood, M. R. & Trevelyan, M. H. (1972) Relationship between physical and psychiatric disorder. *Psychological Medicine*, **2**, 363–372.

Everett, G., de Blois, S., Chang, P. F., *et al* (1983) Effects of cost education, cost audits and faculty chart review on the use of laboratory services. *Archives of Internal Medicine*, **143**, 942–944.

Ferguson, B. & Dudleston, K. (1986) Detection of physical disorder in newly admitted psychiatric patients. *Acta Psychiatrica Scandinavica*, **74**, 485–489.

Fleming, P. R. & Zilva, J. F. (1981) Workloads in clinical pathology: too many tests? *Health Trends*, **13**, 46–49.

Forrest, J. B., Ritchie, W. P., Hudson, M., *et al* (1981) Cost containment through cost awareness. *Surgery*, **90**, 154–158.

Forrest, R. D., Jackson, C. A. & Yudkin, J. S. (1987) The epidemiology of the haemoglobin level – a study of 1057 subjects in general practice. *Postgraduate Medical Journal*, **63**, 625–628.

Fowkes, F. G. R. (1985) Containing the use of diagnostic tests. *British Medical Journal*, **290**, 488–489.

——, Davies, E. R., Evans, K. T., *et al* (1986) Multicentre trial of 4 strategies to reduce the use of a radiological test. *Lancet*, *i*, 367–370.

Gooch, B. R., Isley, W. L. & Utiger, R. D. (1982) Abnormalities in thyroid function tests in patients admitted to a medical service. *Archives of Internal Medicine*, **142**, 1801–1805.

Griner, P. F. & Glaser, R. J. (1982) Misuse of laboratory diagnostic procedures. *New England Journal of Medicine*, **307**, 1336–1339.

Hall, R. C. W., Popkin, M. K., Devaul, R. A., *et al* (1978) Unrecognised physical illness prompting psychiatric admission: a prospective study. *Archives of General Psychiatry*, **35**, 1315–1320.

Hall, R. C. W., Gardner, E. R., Popkin, M. K., *et al* (1981) Unrecognised physical illness prompting psychiatric admission: a prospective study. *American Journal of Psychiatry*, **138**, 629–635.

Hamblin, T. J. (1983) Blood counts and economics. *British Medical Journal*, **286**, 1918–1919.

Hampton, J. R., Harrison, M. J. G., Mitchell, J. R. A., *et al* (1975) Relative contributions of history taking, physical examination and laboratory investigations to diagnosis and management of medical outpatients. *British Medical Journal*, *ii*, 486–489.

—— (1983) The end of clinical freedom. *British Medical Journal*, **287**, 1237–1238.

Hart, G. (1986) Syphilis tests in diagnostic and therapeutic decision making. *Annals of Internal Medicine*, **104**, 368–376.

Hartley, R. M., Charlton, J. R., Harris, C. M., *et al* (1984) Influence of patient characteristics on test ordering in general practice. *British Medical Journal*, **289**, 735–738.

Hecker, R. (1975) Medical practice and multiphasic screening. *Medical Journal of Australia*, **2**, 398–401.

Herridge, C. F. (1970) Physical disorders in psychiatric illness. *Lancet*, *ii*, 949–951.

Hinkle, L. E., & Wolff, H. G. (1957) The nature of man's adaption to his total environment and the relation of this to illness. *Archives of Internal Medicine*, **99**, 442–460.

Hodkinson, H. M. (1981) Value of admission profile tests for prognosis in elderly patients. *Journal of the American Geriatrics Society*, **39**, 206–210.

Howell, R. W. (1970) Smoking habits and laboratory tests. *Lancet*, *ii*, 152.

Kaplan, E. B., Scheiner, L. B. & Boeckmann, A. J. (1985) The usefulness of preoperative laboratory screening. *Journal of the American Medical Association*, **253**, 3576–3581.

Knight, B. (1986) Problems in laboratory medicine. *Medical Protection Society Annual Report*, **94**, 31–32.

Lancet (1979) Psychiatrists with blinkers. *Lancet*, *ii*, 81.

—— (1987) Depression, stress and immunity. *Lancet*, *ii*, 1467–1468.

Latchman, R. W. (1986) Gammaglutamyl transpeptidase and mean corpuscular volume in the assessment of inpatient alcoholics. *British Journal of Psychiatry*, **149**, 353–356.

Leonard, J. V., Clayton, B. E. & Colley, J. R. T. (1975) Use of biochemical profiles in a children's hospital: results of 2 controlled trials. *British Medical Journal*, *ii*, 662–665.

Lloyd, G. G. (1977) Psychological reactions to physical illness. *British Journal of Hospital Medicine*, **18**, 352–358.

Maguire, G. P. & Granville-Grossman, K. L. (1968) Physical illness in psychiatric patients. *British Journal of Psychiatry*, **114**, 1365–1369.

Mills, K. A. & Reilly, P. M. (1983) Laboratory and radiological investigations in general practice. *British Medical Journal*, **287**, 1265–1268.

Moloney, T. W. & Rogers, D. E. (1979) Medical technology – a different view of the contentious debate over costs. *New England Journal of Medicine*, **301**, 1413–1419.

Mooney, G. H. & Drummond, M. F. (1982) Essentials of health economics. *British Medical Journal*, **285**, 949–950.

Murphy, D. L., Goodwin, F. K. & Bunney, W. E. (1971) Leukocytosis during lithium treatment. *American Journal of Psychiatry*, **127**, 1559.

Reuben, D. B. (1984) Learning diagnostic restraint. *New England Journal of Medicine*, **310**, 591–593.

Ritz, E. (1982) Acute hypophosphataemia. *Kidney International*, **22**, 84–94.

Sackett, D. L. (1973) The usefulness of laboratory tests in health screening programs. *Clinical Chemistry*, **19**, 366–372.

Schroeder, S. A. & Showstack, J. A. (1978) Financial incentives to perform medical procedures and laboratory tests. *Medical Care*, **16**, 289–298.

Skinner, H. A., Holt, S., Sheu, W. J., *et al* (1986) Clinical versus laboratory detection of alcohol abuse: the alcohol clinical index. *British Medical Journal*, **292**, 1703–1708.

Sox, H. C., Margulies, I. & Sox, C. H. (1981) Psychologically mediated effects of diagnostic tests. *Annals of Internal Medicine*, **95**, 680–685.

—— & Liang, M. H. (1986) Erythrocyte sedimentation rate-guidelines for rational use. *Annals of Internal Medicine*, **104**, 515–523.

Tarbit, I. F. (1986) Costing clinical biochemistry services as part of an operational management budgeting system. *Journal of Clinical Pathology*, **39**, 817–827.

Thomas, C. J. (1979) The use of screening investigations in psychiatry. *British Journal of Psychiatry*, **135**, 65–72.

Thurow, L. C. (1985) Medicine versus economics. *New England Journal of Medicine*, **313**, 611–614.

White, A. J. & Barraclough, B. (1986) Radiology for psychiatric patients? *British Medical Journal*, **292**, 800–801.

—— & —— (1988) Thyroid disease and mental illness. *Journal of Psychosomatic Research*, **32**, 99–106.

Whitehead, T. P. & Wootton, I. D. P. (1974) Biochemical profiles for hospital patients. *Lancet*, *ii*, 1439–1440.

Willett, A. B. & King, T. (1977) Implementation of laboratory screening procedures on a short term psychiatric inpatient unit. *Diseases of the Nervous System*, **38**, 867–870.

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Brain White-Matter Lesions and Psychosis

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In a prospective study of late-life onset psychosis, five of the first 27 patients studied had extensive white-matter lesions demonstrated by MRI and/or CT. None of 60 age-matched psychiatrically healthy controls demonstrated such lesions. All five patients had a mild dementia and a frontal behavioural syndrome. In addition, every patient performed poorly on neuropsychological tests of frontal function. Dysfunction of the frontal cortex associated with white-matter lesions appears to contribute to the clinical picture of some cases of late-life psychosis.

Late in life, elderly patients can develop a psychiatric picture that resembles schizophrenia. Some accept this as part of the spectrum of schizophrenia (Roth, 1955; Kay & Roth, 1961; Bridge & Wyatt, 1980; Gold, 1984), although others suggest that many patients with late-onset psychosis have organic disease (Leuchter & Spar, 1985). With DSM–III (American Psychiatric Association, 1980), this confusion was partially addressed by classifying any patient with the onset of psychosis after the age of 45 who otherwise would meet criteria for schizophrenia as having 'atypical psychosis'.

In recent years there has been increasing evidence that silent vascular disease may be an important factor in the pathogenesis of some late-life psychoses (LLP). Miller *et al* (1986) described four patients with LLP with no clinical evidence for structural brain disease, who had extensive brain lesions demonstrated by newer neuroimaging techniques. The relationship between these lesions and the psychosis was not certain, and it is possible that they were not causal. For this reason a prospective study comparing patients with LLP with normal age-matched controls was started in an attempt to define better the relationship between structural brain disease and this psychiatric syndrome.

Preliminary results from this study have been reported and the authors (Miller & Lesser, 1988) described a variety of abnormalities in these patients. Approximately half had serious structural brain abnormalities, including tumour, and vascular and post-traumatic lesions involving cortical and/or subcortical structures; the control group of age-matched subjects without a history of major psychiatric problems had no serious abnormalities on magnetic resonance imaging (MRI). Although a variety of brain areas were damaged in the patient group, in the majority the injury involved frontal or subfrontal structures.

The largest subgroup of patients with LLP were those with extensive and confluent lesions in the deep white matter underlying the cortex, demonstrated with MRI and computerised tomography (CT). Five of 27 patients studied had this pathology, which has not previously been reported in LLP. These five patients are described in detail, and the significance of the white-matter lesions in the pathogenesis of the psychosis, a topic which has received little acknowledgement in the literature, is discussed.

Method

Patients with the first onset of psychosis after the age of 45 were evaluated with the following protocol: a psychiatric interview (the Structured Clinical Interview for DSM–III–R (SCID; Spitzer *et al*, 1986)); a medical history; a neurological examination; an EEG; an MRI scan (1.5 Tesla magnet with T_1- and T_2-weighted images); and a CT scan. The Mini-Mental State Examination (MMSE; Folstein *et al*, 1975), Hachinski ischaemia scale (Hachinski *et al*, 1974), Hamilton Rating Scale for Depression (Hamilton, 1967) and Brief Psychiatric Rating Scale (Overall & Gorham, 1962) were administered to help evaluate dementia, risks for cerebrovascular disease, and psychiatric symptoms. Patients were excluded from the study if the MMSE rating was less than 24. A battery of neuropsychological tests was administered, including the Wechsler Adult Intelligence Scale (Satz–Mogel format) (Wechsler, 1981; Adams *et al*, 1984), Wechsler Memory Scale (Wechsler & Stone, 1945), Rey–Osterrieth Complex Figure Test (Osterrieth, 1944), the Wisconsin Card Sort (Berg, 1948), Stroop Test (Stroop, 1935), Consonant Trigrams (Stuss *et al*, 1982), and Verbal Fluency Tests (Benton & Hamsher, 1976). The patients had CT, MRI, and EEG read by experienced neuroradiologists or electroencephalographers, who were blind to subject status.

The patients were compared with 60 age- and sex-matched controls, recruited through an advertisement requesting that normal elderly individuals were wanted for a study on normal ageing. All control subjects had an MRI scan.

Case descriptions

Case 1

An 86-year-old right-handed woman was brought to hospital by her daughter because of increasing paranoia associated with belligerence. Four years earlier, she started to complain that visitors were entering her house at night, and were attempting to steal from her. Also, she developed brief episodes during which she believed her daughter was an imposter, when she would throw objects at the daughter, and would hit her.

There was no history of serious medical problems, and she was not taking medication. She had a history of progressive visual and hearing loss, and was registered as blind.

She was alert but irritable, and was co-operative for only 5–15 minutes at a time. Blood pressure was 190/90 mmHg. She described night-time visitors, but denied that her daughter had been replaced by an imposter. She was orientated to time (month and year), and remembered two of three words over five minutes. Speech and language were normal. Her basic neurological examination was normal, except for absent ankle jerks and severe impairments of vision and hearing. The MMSE score was 26, and the DSM–III–R diagnosis (American Psychiatric Association, 1987) was delusional disorder.

The EEG was normal, but CT showed diffuse cerebral atrophy,. with scattered lacunar infarcts, and diffuse diminished attenuation in the deep white matter underlying the frontal and parietal cortex (Fig. 1). She refused MRI and neuropsychological testing, and was unresponsive to neuroleptics.

Case 2

A 73-year-old man was admitted to hospital after complaining that men who were hired by the CIA wanted to assassinate him and President Reagan. In addition, he no longer cleaned his flat properly. There was no history of significant medical illness.

He was alert and co-operative, with a blood pressure of 155/100 mmHg. He described his delusions in vivid detail, but seemed unconcerned. His affect varied widely from flat to euphoric. He had trouble remembering the exact date, but recalled three of three words after five minutes. Speech, language comprehension, and naming were normal, as was his copying of a three-dimensional drawing. Basic neurological examination was normal, except for significant hearing and visual acuity deficits. His MMSE score was 25, and the DSM–III–R diagnosis was of schizophrenic disorder.

Neuropsychological tests revealed impaired recall of new verbal and non-verbal information. Verbal IQ was 95 and performance IQ was 105. Perseveration errors were noted on tests requiring categorisation or shifting of mental set.

Laboratory investigations, including EEG, were normal. Both CT and MRI (Fig. 2) showed diffuse confluent white-matter lesions, in addition to multiple small lacunae and generalised atrophy. The delusions persisted after treatment with haloperidol.

Case 3

A 72-year-old man was admitted to hospital because he was being increasingly aggressive at his board-and-care home, where he had hit some of his fellow boarders. His personal hygiene had deteriorated, and he had been incontinent

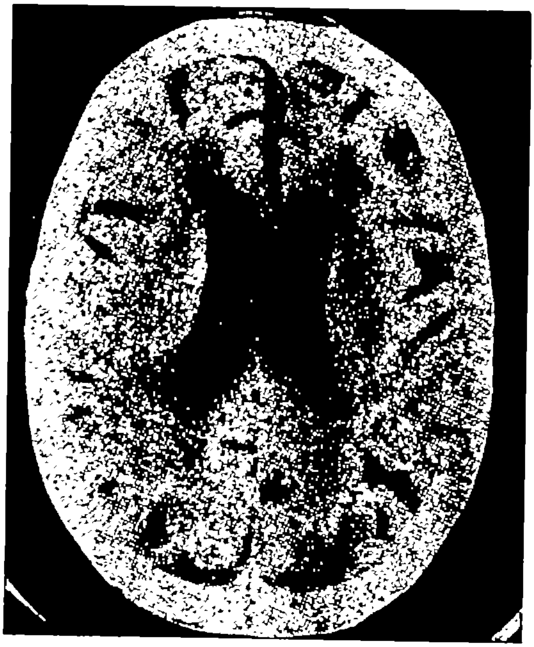

FIG. 1 CT scan from case 1 shows confluent subfrontal and parietal lucencies and atrophy.

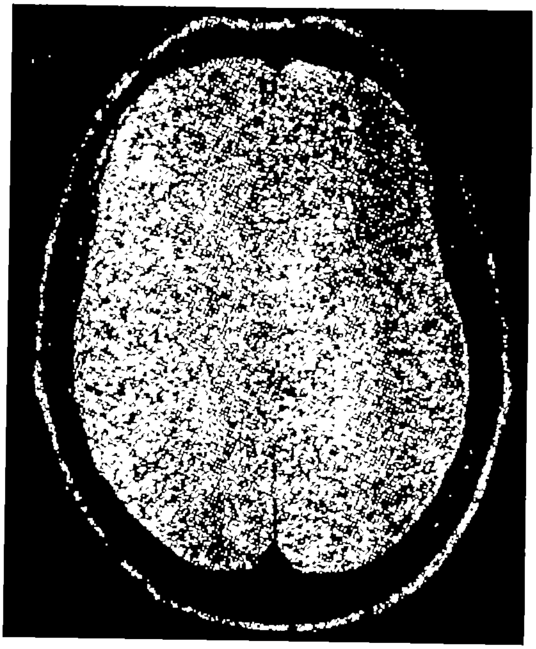

FIG. 2 T_2-weighted MRI scan from case 2 shows increased signal in subfrontal, subparietal, and suboccipital white matter.

on several occasions. He had a long history of hypertension, and was taking several medications, including prazosin (1 mg/t.i.d), temazepam (30 mg q.h.s), L-thyroxine (0.1 mg q.d.), and carbidopa with L-dopa (25/250 tablets q.i.d.). Four years earlier, he had a coronary artery bypass and had a pacemaker inserted.

He was pleasant and co-operative. He repeatedly complained that someone had inserted a doorknob under his skin at the site of the cardiac pacemaker, but seemed unconcerned about this. He knew the month and year but not the day, and could not remember three words for five minutes. He could not name low-frequency objects (e.g. 'door hinge'), and followed two-step but not three-step commands. Motor tone was increased, and a coarse rapid tremor was noted. Gait was wide based and slow, and toes were downgoing. His MMSE score was 24, and his psychiatric diagnosis was of delusional disorder.

Neuropsychological testing revealed impairment in learning and some responses were confabulatory. Mild impairment of constructional and mathematical abilities were present. Verbal and performance IQ were 74.

The CT scan showed multiple subcortical white-matter lucencies, and several lacunar infarcts in the basal ganglia. The patient's delusional syndrome did not respond after the L-dopa was decreased, and he was discharged to a nursing home.

Case 4

A 62-year-old right-handed man was admitted to hospital to assess a memory disturbance associated with paranoia and delusions. In the months before admission, he began to accuse others of trying to steal his money. There was a past history of diabetes, hypertension, hearing loss, and a vague history of stroke in the year before admission.

The patient had a blood pressure of 160/92 mmHg. He repeatedly stated that people had stolen from him at work. Although irritable and easily angered, at times he was euphoric. The basic neurological examination was normal, except for mild dysmetria and a wide-based ataxic gait, and a moderate sensorineural-type hearing loss was demonstrated. His psychiatric diagnosis was of delusional disorder.

His full-scale IQ was 88, with a significant discrepancy between verbal (95) and performance IQ (78). Verbal and non-verbal memory skills, visual perceptual and constructional abilities, frontal systems, and attentional abilities all were impaired. In contrast, language skills, mathematical ability, and general information were within the low to high average range.

The EEG was normal, but the CT scan showed multiple lacunae in the deep white matter and basal ganglia. He did not respond to drug therapy.

Case 5

A 68-year-old right-handed man was referred to hospital after an attempt to have sexual relations with a 13-year-old niece, a behaviour that seemed 'out of character'. Before admission he had become increasingly disinhibited, and had stated that he had heard God speaking to him. Also, he insisted that he was a captain in the merchant marines, although this was not true. There was a complicated medical history, with chronic obstructive pulmonary disease, diabetes, hypertension, and heart disease. His medications included ibuprofen (400 mg t.i.d.), chlorpropamide (250 mg t.i.d.), clonidine (2 mg t.i.d.), aminophylline (200 mg b.i.d.), digoxin (25 mg q.d.), and furosemide (40 mg q.d.).

He was disinhibited, with pressured speech and flight of ideas. He fluctuated between irritability, anger, and euphoria. The delusions were described with detachment and lack of emotion. He had trouble with memory tasks, but language was fluent and comprehension was good. Basic neurological examination was normal, with the exception of severe sensorineural hearing loss, and moderate visual disturbance secondary to bilateral cataracts. The psychiatric diagnosis was of bipolar disorder, manic phase with psychotic features.

The CT scan showed well circumscribed lucencies, which seemed to undercut both frontal and parietal lobes. His behaviour did not improve with neuroleptics, and he was discharged to a nursing home.

Discussion

The five elderly patients described here were all seen because of a behavioural disorder associated with prominent delusions. Although two of the patients showed minor neurological deficits (cases 3 and 4), only one of these had a history of stroke. Hypertension was present in four of the five patients, and serious deafness and/or visual deficits in three. Intellectual impairment was not recognised as a major problem by the patients' families or primary health care personnel, yet neurobehavioural and neuropsychological batteries did demonstrate evidence for dementia in every patient. However, language function was normal, and the dementia syndrome was not apparent unless special tests assessing frontal lobe and memory function were performed.

The clinical features of these patients differed from those seen in classic schizophrenia: none had a prior history of psychiatric illness, nor was there evidence of a formal thought disorder, yet each had complex delusions with or without hallucinations. Unshakable delusions were a prominent feature of the psychiatric presentation, and although difficult to quantify, all had relative sparing of personality. Three had a DSM-III-R diagnosis of delusional (paranoid) disorder, one met criteria for schizophrenia, and one had a manic syndrome. Although there was some variability in the specific psychiatric presentations, all patients had strikingly similar large subfrontal white-matter lesions on CT and MRI.

Considering all the clinical and radiographic data, these conditions could be rediagnosed as organic delusional or organic affective disorders, but this diagnostic information was not apparent upon entry to the study, when the clinician initially evaluated the patient. In several cases, the additional testing was pursued only because the patient was a study participant.

Lesions in the frontal regions and behavioural abnormalities

It is well recognised that frontal-lobe lesions may produce changes in behaviour, but may be otherwise neurologically silent (Stuss & Benson, 1984). Although none of the patients had lesions evident in the frontal lobes, all had extensive subfrontal white-matter infarction. In two patients (cases 1 and 5), the white matter underlying the frontal lobe was the predominant site of abnormality, and this region was involved in all five cases. Subcortical white-matter lesions can disconnect the frontal areas from the remaining brain, and white-matter diseases such as metachromatic leucodystrophy often start with behavioural changes that include frontal-lobe symptoms and sometimes mimic schizophrenia (Skomer *et al*, 1983).

Irritability, apathy, behavioural disinhibition, and poor judgement, symptoms commonly associated with frontal-lobe injury, were present in all the patients, and euphoria was present in four. All were brought to hospital because of behavioural disinhibition associated with impairment of judgement. It can be argued that in every patient this aspect of their psychiatric syndrome and not the delusions was the major source of concern to family and friends. Irritability and apathy were also present, and in all but case 1, this was seen to fluctuate with periods of euphoria. The group did poorly on tests of frontal function and on the battery of frontal tests, suggesting that the frontal lobes and/or their connections were injured. These findings support a role for the frontal cortex in the pathogenesis of some of the abnormal behaviour seen in LLP.

Delusions as part of a frontal syndrome

Although delusions and hallucinations are not typically indicators of frontal damage, specific delusions have been reported in association with such lesions. Reduplicative paramnaesia syndrome was first described by Pick (1903) in a patient with Alzheimer's disease "who insisted that the hospital she was in was located in her own community rather than in the city of its actual location". It has since been noted that many patients with reduplicative paramnesia have periventricular and right hemisphere dysfunction (Weinstein & Kahn, 1955), and Benson *et al* (1976) described three patients recovering from head traumas with a combination of right hemisphere and bifrontal abnormality who had classic reduplicative paramnesia. Another dramatic delusion which has been described following frontal injury is the Capgras syndrome (Alexander *et al*, 1979), which features the belief that a person close to the patient has been replaced by one or more identical appearing imposters (a feature of case 1). A third syndrome which may approach delusional proportions and which may be seen in patients with frontal damage is confabulation, particularly the 'fantastic' or 'spontaneous' confabulation syndrome (Stuss *et al*, 1978). Even where the degree of confabulation is less pronounced, Mercer *et al* (1977) demonstrated that a consistent clinical feature was a lack of self-criticism, and they postulated a frontal dysfunction.

In each of these three syndromes, the patient presents an incorrect response and maintains the response in the face of contrary evidence. Inability to monitor and self-correct appears to be the primary dysfunction underlying these delusions. In all five of the cases described above, there was a striking inability to monitor and self-correct, and the delusions were part of a more generalised frontal syndrome.

Sensory deprivation has been described as a risk factor for LLP, with 38% of subjects suffering from significant hearing loss compared with 18% of patients with late-life affective disease (Cooper & Curry, 1975). Two of our patients had serious visual and hearing loss, a third patient had mild sensorineural deafness, whereas two had no sensory deficits. The role of the sensory deficits in the pathogenesis of the psychosis is uncertain, and it is possible that the sensory disturbance in conjunction with the mental impairment contributed to the hallucinations and delusions which were present in four of the five patients. Sensory deprivation is common in the elderly and can lead to modality-specific hallucinations, but delusional affirmation of the hallucination is unusual (Cummings & Miller, 1987), and the frontal and subfrontal brain injury appeared to be an important contributor to the psychosis in our cases.

Aetiology of the white-matter lesions

With third-generation CT and, more recently, MRI, it has become increasingly clear that many elderly people have subtle abnormalities in the white matter underlying cortex. In one study, 88% of demented elderly subjects compared with 61% of non-demented patients with ischaemic vascular disease had at least one lesion in the white matter (Hershey *et al*, 1987). Bradley *et al* (1984) noted small lesions in 30% of all patients over the age of 65; these lesions were not common in younger patients. Some have suggested that these lesions are small white-matter infarctions (Brant-Zawadzki *et al*, 1985). It has been demonstrated that hypertension is present in a higher proportion of patients with these defects than in age-matched controls, suggesting a possible vascular aetiology (Brant-Zawadzki *et al*, 1985). Their clinical significance is debated (Hackinski *et al*, 1987), with suggestions that they correlate with dementia (Brant-Zawadzki *et al*, 1985) or even are asymptomatic (Hershey *et al*, 1987).

Although small lesions may be asymptomatic, larger ones often are associated with dementia (Goto *et al*, 1981; Steingart *et al*, 1987). Some of the original papers on this topic noted that delusions were present in some of the patients (Goto *et al*, 1981; Tomonaga *et al*, 1982), although the psychiatric features of white-matter lesions have not been extensively characterised, and in most cases have been ignored. We have not seen large subfrontal lesions in the 60 control patients that we have so far studied, and doubt that lesions as extensive as those seen in our five patients are asymptomatic or unrelated to their neuropsychiatric presentation.

These five cases demonstrate that the first and primary clinical manifestations of white-matter lesions may be psychiatric. The relationship of these lesions in the subfrontal area to frontal dysfunction needs further study, but in these five cases frontal dysfunction was profound. Neurophysiological studies such as computerised EEG and single-photon emission computerised tomography (SPECT) may clarify the relationship between white-matter lesions and frontal function. Because these lesions are common in the elderly, further study of their clinical significance will be important.

When psychosis appears for the first time in late life, a careful search for organic illness, incorporating CT or MRI, should be undertaken. In particular, a subset of patients with white-matter lesions may present with both delusions and a frontal syndrome.

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References

Adams, R. L., Smigielski, J. & Jenkins, R. L. (1984) Development of a Satz-Mogel short form of the WAIS-R. *Journal of Consulting and Clinical Psychology*, **52**, 908.

Alexander, M. P., Stuss, D. T. & Benson, D. F. (1979) Capgras syndrome: a reduplicative phenomenon. *Neurology*, **29**, 334–339.

American Psychiatric Association (1980) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn) (DSM-III). Washington, DC: APA.

—— (1987) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn, revised) (DSM-III-R). Washington, DC: APA.

Benson, D. F., Gardner, H. & Meadows, J. C. (1976) Reduplicative paramnesia. *Neurology*, **26**, 147–151.

Benton, A. L. & Hamsher, K. deS (1976) *Multilingual Aphasia Examination*. Iowa City: University of Iowa.

Berg, E. A. (1948) A simple objective test for measuring flexibility in thinking. *Journal of General Psychology*, 39, 15–22.

Bradley, W. G., Waluch, V., Brant-Zawadzki, M., *et al* (1984) Patchy, periventricular white matter lesions in the elderly: a common observation during NMR imaging. *Noninvasive Medical Imaging*, **1**, 35–41.

Brant-Zawadzki, M., Fein, G., Van Dyke, C., *et al* (1985) MR imaging of the aging brain: patchy white-matter lesions and dementia. *American Journal of Neuroradiology*, **6**, 675–682.

Bridge, P. T. & Wyatt, R. J. (1980) Paraphrenia: paranoid states of late life. I. European research. *Journal of the American Geriatric Society*, **28**, 193–200.

Cummings, J. L. & Miller, B. L. (1987) Visual hallucinations: an overview. *Western Journal of Medicine*, **146**, 46–51.

Cooper, A. F. & Curry, A. R. (1975) The pathology of deafness in the paranoid and affective psychoses of later life. *Journal of Psychosomatic Research*, **20**, 97–105.

Folstein, M. F., Folstein, S. E. & McHugh, P. R. (1975) "Mini-Mental State": a practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, **12**, 185–198.

Gold, D. (1984) Late age of onset schizophrenia: present but unaccounted for. *Comprehensive Psychiatry*, **25**, 225–237.

Goto, K., Ishii, N., & Fukasawa, H. (1981) Diffuse white-matter disease in the geriatric population. *Radiology*, **141**, 687–695.

Hachinski, V. C., Lassen, N. A. & Marshall, J. (1974) Multi-infarct dementia. A cause of mental deterioration in the elderly. *Lancet*, *ii*, 207–210.

Hachinski, V. C., Potter, P. & Merskey, H. (1987) Leuko-araiosis. *Archives of Neurology*, **44**, 21–23.

Hamilton, M. (1967) Development of a rating scale for primary depressive illness. *British Journal of Social and Clinical Psychology*, **6**, 270–296.

Hershey, L. A., Modic, M. T., Greenough, P. G., *et al* (1987) Magnetic resonance imaging in vascular dementia. *Neurology*, **37**, 29–36.

Kay, D. W. K. & Roth, M. (1961) Environmental and hereditary factors in the schizophrenia of old age ("late paraphrenia") and their bearing on the general problem of causation in schizophrenia. *Journal of Mental Science*, **17**, 649–686.

Leuchter, A. F., & Spar, J. E. (1985) The late-onset psychoses. Clinical and diagnostic features. *Journal of Nervous and Mental Disease*, **173**, 488–493.

Mercer, B., Wapner, W., Gardner H., *et al* (1977) A study of confabulation. *Archives of Neurology*, **34**, 429–433.

Miller, B. L., Benson, D. F., Cummings, J. L., *et al* (1986) Late-onset paraphrenia: an organic delusional system. *Journal of Clinical Psychiatry*, **47**, 204–207.

—— & Lesser, I. M. (1988) Late-life psychosis and modern neuroimaging. In *Psychiatric Clinics of North America* (ed. D. Jeste). Philadelphia: W. B. Saunders.

OSTERRIETH, P. A. (1944) Le test de copie d'une figure complexe. *Archives de Psychologie*, **30**, 206–356.

OVERALL, J. W. & GORHAM, D. R. (1962) The Brief Psychiatric Rating Scale. *Psychological Research*, **10**, 795–812.

PICK, A. (1903) Clinical studies: III. On reduplicative paramnesia. *Brain*, **26**, 260–267.

ROTH, M. (1955) The natural history of mental disorder in old age. *Journal of Mental Science*, **129**, 281–301.

SKOMER, C., STEARS, J. & AUSTIN, J. (1983) Metachromatic leukodystrophy (MLD) adult MLD with focal lesions by computerized tomography. *Archives of Neurology*, **40**, 354–355.

SPITZER, R. L., WILLIAMS, J. B. & GIBBON, M. (1986) Structured Clinical Interview for DSM-III-R Patient Version (SCID 8/1/86). New York: New York State Psychiatric Institute.

STEINGART, A., HACHINSKI, V., LAU, C., *et al* (1987) Cognitive and neurologic findings in subjects with diffuse white matter lucencies on computed tomographic scan (leuko-araiosis). *Archives of Neurology*, **44**, 32–35.

STROOP, J. (1935) Studies of interference in serial verbal reactions. *Journal of Experimental Psychology*, **18**, 643–661.

STUSS, D. T., ALEXANDER, M. P., LIEBERMAN, A., *et al* (1978) An extraordinary form of fantastic confabulation. *Neurology*, **28**, 1166–1172.

——, KAPLAN, E. F., BENSON, D. F., *et al* (1982) Evidence for the involvement of orbitofrontal cortex in memory functions: an interference effect. *Journal of Comparative Physiological Psychology*, **96**, 913–925.

—— & BENSON, D. F. (1984) Neuropsychological studies of the frontal lobes. *Psychological Bulletin*, **95**, 3–28.

TOMONAGA, M., YAMANOUCHI, H., TOGHI, H., *et al* (1982) Clinicopathologic study of progressive subcortical vascular encephalopathy (Binswanger type) in the elderly. *Journal of the American Geriatric Society*, **30**, 524–529.

WECHSLER, D. (1981) Wechsler Adult Intelligence Scale–Revised. New York: Psychological Corporation.

—— & STONE, C. (1945) *Wechsler Memory Scale*. New York: Psychological Corporation.

WEINSTEIN, E. A. & KAHN, R. L. (1955) *Denial of Illness: Symbolic and Physiological Aspects*. Springfield: Charles C. Thomas.

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Mood Changes After Right-Hemisphere Lesions

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Ninety-three patients with acute stroke lesions restricted to the right hemisphere were examined for the presence of mood changes. While 46 patients showed no mood changes, 19 were unduly cheerful, 17 had developed major depression, and 11 had developed minor depression. Although there were no significant between-groups differences in other demographic variables, neurological deficits, activities of daily living, cognitive impairment, or quality of social support, patients with major depression had a significantly higher frequency of familial history of psychiatric disorder and lesions of the parietal cortex than patients with either no mood change or major depression following left-hemisphere lesions. On the other hand, undue cheerfulness was significantly associated with lesions of the right frontal operculum. These findings suggest that major depression following right-hemisphere lesions may have a different aetiology and mechanism than major depression following left frontal or basal ganglia lesions.

In previous studies of post-stroke mood disorders, we have consistently found significant associations between left anterior brain injury and major depression (Robinson *et al*, 1984; Starkstein *et al*, 1987*a*). Although this association between left-hemisphere lesions and either depression or a negativistic affective state has been reported by numerous studies (Gainotti, 1972; Gasparrini *et al*, 1978; Finklestein *et al*, 1982), some investigators have found a high frequency of depression associated with right- as well as left-hemisphere injury (Folstein *et al*, 1977; Sinyor *et al*, 1986). We have suggested (Robinson *et al*, 1987) that the failure to find a lateralised emotional response to injury may be due to methodological differences between studies in variables such as time since injury (lateralised differences are more evident during the acute post-stroke period), intrahemispheric lesion location (lateralised differences are more evident with anterior than posterior brain injury), or prior brain injury (the most recent injury does not predict severity of depression) (Lipsey *et al*, 1983).

The formulation, however, that these methodological variables are important in determining the relative frequency of depression following right-hemisphere injury, does not address the fundamental issue of whether the aetiology of depression associated with right- and left-hemisphere lesions may be different. Since we have described the phenomenology, natural course, and relationship to location of injury for depressive disorders associated with left-hemisphere lesions extensively in previous publications, the present study focuses on mood disorders associated with right-hemisphere injury.

We report here the results of an evaluation of 93 patients with right-hemisphere strokes for the presence of mood changes (depression and undue cheerfulness) and their association with predisposing factors.

Method

Study population

Patients included in this study were selected from two hospital populations: (a) 254 consecutive admissions to the University of Maryland Hospital for treatment of acute thromboembolic infarction or intracerebral haemorrhage, and (b) a consecutive series of 68 patients admitted to the Montebello Rehabilitation Hospital for therapy following a cerebral infarct or haemorrhage. Patients with decreased consciousness (stupor or coma) or severe comprehension deficits (as determined by an independently administered standardised neurological examination and the finding that patients did not score within ten points on test–retest administration of the Zung Depression Scale) were excluded from the study.

For the present investigation, we included two groups of patients: (a) patients who had single right-hemisphere strokes based on CT findings and/or clinical diagnosis, and (b) a consecutive series of patients who developed major depression following left-hemisphere strokes. CT scans were performed in all patients included in the study. Patients with a previous history of stroke were excluded from the study.

Neurological and psychiatric examination

The neurological examination and diagnosis for all University of Maryland patients (72 with right-hemisphere lesions and 24 with left-hemisphere lesions) was done using the criteria established by the Stroke Data Bank of the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) (Kunitz *et al*, 1984). Patients at Montebello Hospital (21 with right-hemisphere lesions and 3 with left-hemisphere lesions) received a standard clinical neurological examination. All neurological examinations were performed blind to findings on psychopathological examination.

After giving informed consent, patients were administered a series of standardised quantitative measures of mood, cognitive function, and physical impairment. We have previously shown that these instruments give reliable and valid measurements in this stroke population (Robinson & Benson, 1981; Robinson & Szetela, 1981; Robinson *et al*, 1983). Examinations were administered in a private room between 11.00 a.m. and 2.00 p.m. to minimise any possible effect of diurnal mood variation. The Hamilton Rating Scale for Depression (HRSD; Hamilton, 1960), a 17-item questionnaire measuring psychological and physiological symptoms of depression, was filled out by the interviewer. The Zung Self-Rating Depression Scale (Zung, 1965), a 20-item questionnaire, was read to each patient and his/her responses were scored using the four Zung categories. The modified Present State Examination (PSE; Wing *et al*, 1974), a semistructured psychiatric interview that elicits symptoms related to depression and anxiety, was scored by the examiner. The Mini-Mental State Exam (MMSE; Folstein *et al*, 1975) and the Johns Hopkins Functioning Inventory (JHFI; Robinson *et al*, 1983) were also administered to each patient. The MMSE is an 11-item examination that has been found to be reliable and valid in assessing a limited range of cognitive functions in stroke patients (Folstein *et al*, 1975; Robinson *et al*, 1986). Scores may range from 0 to 30 and a score of 23 or below indicates cognitive impairment. The JHFI contains ten items and evaluates degree of independence in activities of daily living such as walking, dressing, and eating (Robinson *et al*, 1983). Scores range from 0 to 27, and higher scores indicate greater degrees of impairment. Social functioning was quantified both by number of social connections using the Social Ties Checklist (STC) (maximum score of 10) and by personal satisfaction with social relations using the Social Functioning Exam (SFE) (scores range from 0 to 1000, with higher scores indicating poorer social functioning) (Starr *et al*, 1983).

Psychiatric diagnosis was established using DSM–III (American Psychiatric Association, 1980) symptom criteria for major depression or minor (dysthymic) depression. The symptoms used for these diagnostic criteria were elicited by the PSE. The method used to convert PSE symptoms to DSM–III major or minor depression diagnosis is available upon request. Undue cheerfulness was also determined from symptoms elicited by the PSE. The criteria for undue cheerfulness were as follows: a self-report of an elevated or expansive mood; or a clinical observation of inappropriate cheerfulness or elation, and a self-report of no feelings of sadness or depression.

Based on the hand used for writing, patients were considered right-handed, left-handed or mixed-handed.

While patients were interviewed generally within the second or third week after stroke, no interview was carried out after 60 days post-stroke.

CT scan examination

CT scans were read by one of us (SES) who was blind to the clinical findings. All CT scans had a consistent slice thickness and angle to the canthomeatal line. The damaged area was localised in specific brain regions following the procedure of Levine & Grek (1984). Lesion volume (expressed as a percentage of total brain volume) was calculated from the ratio of the largest cross-sectional area of the lesion on any CT-scan slice to the cross-sectional area of the whole brain on the slice passing through the body of the lateral ventricles. We have previously demonstrated the reliability of this procedure and its high correlation with other methods of determining lesion volume (Robinson *et al*, 1986).

Statistical analysis

Statistical analysis was carried out using means and standard deviations, analysis of variance (ANOVA) and Pearson correlation coefficients. Frequency distributions were analysed using χ^2 tests with Yates' modification for expected cell sizes below 5.

Results

Background characteristics

Demographic data are presented in Table I. The study population consisted mainly of males in their late 50s and early 60s. There was a slight preponderance of blacks, and the population was primarily from lower socioeconomic classes (i.e. Hollingshead class IV and V).

Although we did not obtain detailed family histories using multiple informants (Andreasen *et al*, 1977) we did obtain as much information about family history as we could from the patients and/or relatives who were available at the time of interview. The distribution of positive familial history of psychiatric disorder for first- and second-degree relatives (alcoholism (55%) and depression (45%)) was significantly different between the four groups ($\chi^2 = 7.7$, d.f. = 3, $P < 0.05$); and on individual comparisons, patients with major depression had a significantly higher frequency of positive family history of psychiatric disorder than patients with no mood disorders (χ^2 Yates = 4.08, d.f. = 1, $P < 0.05$). Although there was also a trend for major and minor depressed patients to show higher frequencies of positive personal psychiatric history ($\chi^2 = 6.3$, d.f. = 3, $P = 0.09$), it did not reach statistical significance. Personal histories were positive for alcoholism and anxiety, while only one patient had a previous history of depression. No other significant differences were observed in the remaining demographic variables (Table I).

In order to establish if this higher frequency of family psychiatric history was specific for major depression following right-hemisphere lesions, we compared this group of patients with a consecutive series of 27 patients who developed major depression following left-hemisphere lesions (Table I). Patients with major depression following right-hemisphere lesions showed a significantly higher frequency of positive family history of psychiatric disorder than major depressed patients following left-hemisphere lesions (one patient had a family history of anxiety disorder in a first-degree relative) (χ^2 Yates = 4.44, d.f. = 1, $P < 0.05$).

TABLE I
Demographic data

	Right hemisphere				*Left hemisphere*
	No depression	*Undue cheerfulness*	*Major depression*	*Minor depression*	*Major depression*
Number of patients	46	19	17	11	27
Age: years					
mean	64	60	60	62	56
s.d.	10	14	11	8	13
Sex: % females	35	42	47	36	52
Race: % blacks	65	74	41	55	59
Socio-economic status: Hollingshead class IV or V	87	74	82	82	89
Marital status: % married	54	37	42	36	44
Handedness: % right-handed	87	90	100	100	89
Education: years					
mean	6.5	8.2	8.4	8.8	9.3
s.d.	3.7	4.3	3.4	3.5	2.8
Familial history of psychiatric disorders: % positive*	6	5	29	9	4
Personal history of psychiatric disorders: % positive	15	5	29	36	6
Time since stroke: days					
mean	13.1	11.2	16.0	20.9	14.5
s.d.	12.7	6.5	9.4	18.6	11.4

*$P < 0.05$.

TABLE II
Scores of depression, cognitive impairment, activities of daily living and social functioning[1]

	No depression	*Undue cheerfulness*	*Major depression*	*Minor depression*
Number of patients	46	19	17	11
Depression scores				
PSE[2]	4.0 (3.0)	8.3 (4.5)	23 (9.2)	15 (7.5)
HRSD[3]	5.0 (4.1)	5.6 (3.1)	15.2 (5.3)	12.2 (5.3)
Zung[4]	36 (6.7)	36 (5.4)	57 (9.3)	45 (9.0)
Activities of daily living				
JHFI	5.6 (4.6)	5.2 (6.2)	7.7 (4.9)	5.8 (5.7)
Cognitive impairment				
MMSE	24 (4.6)	23 (6.3)	23 (5.6)	24 (6.1)
Social functioning				
SFE	251 (163)	291 (201)	332 (217)	358 (272)
STC	3.5 (1.6)	4.3 (1.8)	4.3 (2.1)	3.8 (1.9)

1. Standard deviations are in parentheses.
2. $F = 51.2$, d.f. $= 3, 88$, $P < 0.001$.
3. $F = 26.5$, d.f. $= 3, 88$, $P < 0.001$.
4. $F = 34.4$, d.f. $= 3, 88$, $P < 0.001$.

No significant differences were found in the remaining demographic variables (Table I).

Neurological findings

There were no significant differences in the frequency of motor or sensory impairments among the four groups. Most patients had a hemiparesis (91%, 84%, 94% and 100% for non-depressed, unduly cheerful, major and minor depressed patients, respectively), and about half had sensory deficits (59%, 47%, 31% and 0%, respectively). A smaller proportion showed visual-field disturbances (26%, 5%, 19% and 0%, respectively), neglect (17%, 11%, 13% and 0%, respectively) and dysarthria (22%, 11%, 19% and 18%, respectively).

Depression scores, physical impairment, cognitive impairment and social function

As expected, patients with major depression showed the highest depression scores, while patients with minor depression had scores between those of the major depressed and the non-depressed patients (Table II).

There were no significant between-group differences in scores of cognitive impairment (MMSE), activities of daily living (JHFI), social functioning (SFE) and social ties (STC) (Table II).

There were no significant correlations between PSE scores and scores of cognitive impairment (PSE v. MMSE, $r = 0.15$), activities of daily living (PSE v. JHFI, $r = 0.23$), social functioning (PSE v. SFE, $r = 0.13$) or social ties (PSE v. STC, $r = 0.13$).

CT scan findings

Fifty-four patients had positive CT scans (Table III). The lesions were mainly ischaemic infarctions, and the distribution of infarcts and haemorrhages was not significantly different between the four groups (Table III). There were also no significant between-group differences in lesion volumes ($F = 0.96$, NS) (Table III). Patients with undue cheerfulness, however, showed a significantly higher frequency of lesions involving the frontal operculum compared with (major and minor) depressed and non-depressed patients ($\chi^2 = 6.17$, d.f. $= 2$, $P < 0.05$). On individual comparisons, patients with undue cheerfulness showed a significantly higher frequency of frontal opercular lesions than patients with (major and minor) depression (χ^2 Yates $= 3.88$, d.f. $= 1$, $P < 0.05$). On the other hand, patients with depression (both major and minor) showed a significantly higher frequency of lesions involving the parietal cortex than the other two groups ($\chi^2 = 9.60$, d.f. $= 2$, $P = 0.022$) (Table III). On individual comparisons, the depressed patients (major and minor) had a significantly higher frequency of parietal lesions than the unduly cheerful patients ($\chi^2 = 9.21$, d.f. $= 1$, $P < 0.01$).

Although there were more depressions associated with posterior (parietal) than anterior lesions, there was no significant correlation between the distance of anterior lesion border from the frontal pole and severity of depression (PSE v. anterior border, $r = 0.05$) or between the distance of posterior lesion border from the frontal pole and severity of depression (PSE v. posterior border, $r = 0.01$). In addition, there was no significant correlation between lesion volume and severity of depression (PSE v. lesion volume, $r = 0.10$).

Discussion

In the present study, we have examined the type and frequency of mood changes following right-hemisphere strokes. During the acute post-stroke period, almost one-third of the patients developed depression (minor or major), while almost a quarter developed undue cheerfulness. Patients with major depression had a significantly higher frequency of

TABLE III
Lesion location (number of patients)

	No depression	*Undue cheerfulness*	*Major depression*	*Minor depression*
Number of patients with positive CT scans	25	12	9	8
Ischaemic strokes	22	11	7	7
Frontal dorsolateral	1	0	2	4
Frontal opercular	4	5	0	1
Temporal lobe	7	1	2	0
Parietal lobe	9	1	6	5
Occipital lobe	7	1	3	0
Basal ganglia	6	6	2	1
Thalamus	4	1	0	0
Internal capsule	2	5	0	0
Corona radiata	1	1	1	2
Lesion volume				
mean	9.0	6.2	10.0	7.4
s.d.	6.3	4.0	5.1	6.5

familial history of psychiatric disorder than patients with right-hemisphere lesions without major depression, or patients with major depression following left-hemisphere lesions. Depressed patients with right-hemisphere lesions also had a significantly higher frequency of lesions in posterior (mainly parietal) cortex than non-depressed or unduly cheerful patients. On the other hand, patients with undue cheerfulness showed a significantly higher frequency of lesions involving the frontal operculum.

Before further discussion, several limitations of this study should be pointed out. While family histories were obtained from patients and/or relatives, systematic interrogation using multiple informants was not carried out. Thus it is probable that the frequency of familial psychiatric history was underestimated, and it is also possible that the presence of depression may have biassed the report of a positive familial psychiatric history. The present findings therefore need to be replicated using multiple-informant family pedigrees (Andreasen *et al*, 1977). It should be emphasised, however, that these methodological limitations should have affected all groups equally and that they are not an explanation of why familial disorders were more frequent with right-hemisphere major depression than left-hemisphere major depression.

Another limitation is that the diagnosis of undue cheerfulness was not based on standard criteria, as unduly cheerful patients do not meet DSM-III criteria for hypomania. Notwithstanding, this phenomenon of euphoria or elation has for many years been reported in patients with right-hemisphere lesions (Gainotti, 1972; Cutting, 1978). Although no diagnostic criteria have been established for this phenomenon, we defined undue cheerfulness based on either the presence of a self-report of an expansive or elated mood (74% of the patients with undue cheerfulness had this symptom) or the clinical observation of inappropriate cheerfulness or excitement (26% of the patients). Although not a part of our criteria for undue cheerfulness, flight of ideas and increased energy were present in 37% of the unduly cheerful patients, while 11% had grandiose ideas.

Questions that now arise are, first, what is the pathogenesis of depression in patients with right-hemisphere lesions, and second, is this pathogenesis different from that in patients with left-hemisphere lesions? There were no significant differences between depressed and non-depressed patients in terms of important demographic variables, such as age, sex, race, education and socio-economic status. Moreover, there were no significant between-group differences in scores of physical impairment, cognitive deficits, social functioning or social ties. The finding that patients with major depression following right-hemisphere lesions had a significantly higher frequency of family history of psychiatric disorder suggests that hereditary factors may play an important role in the production of major depression following right-hemisphere lesions, at least for a subgroup of patients.

Lesion location also seemed to play an important role in the production of depression, and the finding of a significantly higher frequency of depression following lesions in posterior cortical areas replicates our previous findings in a much smaller population (Robinson *et al*, 1984), and also agrees with findings of other investigators (Finset, 1988).

We have previously suggested that left anterior lesions may lead to depression by disrupting biogenic amine pathways, and that the correlation between severity of depression and proximity of the lesion to the frontal pole is a result of interrupting these pathways closer to their 'downstream' origin in the frontal pole. How parietal lesions in the right hemisphere may lead to depression is uncertain. However, the findings do suggest that the mechanism which produces major depression after right-hemisphere lesions may be different from those which lead to major depression after left anterior lesions.

Ross & Rush (1981) reported the case of a patient with a right temporo-parietal infarction who denied being depressed, but showed autonomic symptoms of depression and a depressive affect. A dexamethasone suppression test showed non-suppression and the depressive symptoms improved after treatment with tricyclic antidepressants. Based on these findings, Ross and colleagues have hypothesised that a patient's denial of depression may be secondary to the inability of mood information (generated in the right hemisphere by structures which were not involved by the lesion) to reach the verbally-expressive left hemisphere. They have suggested that expression and comprehension of emotions are organised in the right hemisphere in an analogous fashion to language in the left hemisphere. Although we did not examine our patients for disturbances in recognition or expression of emotion, we did find depression to be significantly associated with lesions in the parietal lobe. We require that a diagnosis of major depression includes the patient's admission that he or she is feeling depressed or sad. Thus, all patients we examined with major depression and parietal involvement clearly acknowledged internal feeling of depression. The extent to which aprosodic disturbances may interfere with the diagnosis of mood disorders in patients with right-hemisphere injury, however, is uncertain. This issue will need to be examined systematically in another study.

The other mood change that was frequently identified among patients with right-hemisphere lesions was inappropriate cheerfulness, which was associated with lesions involving the right frontal operculum. Previous studies have found that lesions of the frontal cortex, mainly in the right hemisphere, are associated with elevated mood (Oppenheim, 1890; Kleist, 1931; Rylander, 1939; Starkstein *et al*, 1987*b*). We have suggested (Starkstein *et al*, 1987*b*) that these mood disorders may be related to disruptions in frontal cortical interaction with the limbic system, particularly the amygdala, septum, hypothalamus and mesencephalon (Nauta, 1971).

In conclusion, right-hemisphere strokes were associated with a high frequency of mood changes. Depression was associated with both genetic factors and lesions in posterior cortical areas, while undue cheerfulness was associated with lesions in the frontal operculum. Since demographic factors, neurological symptoms, severity of physical impairment, cognitive deficits and social support did not explain the presence of depression or undue cheerfulness, these findings suggest that mood changes following right-brain lesions (as with left-hemisphere lesions) are not simply an understandable consequence of the impairment but may be the result of more complex biological processes. The neurophysiological mechanisms leading to major depression, however, may be different for left frontal/basal ganglia injury as compared with right parietal or brainstem injury (Starkstein *et al*, 1988).

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References

AMERICAN PSYCHIATRIC ASSOCIATION (1980) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn). Washington DC: APA.

ANDREASEN, N., ENDICOTT, J., SPITZER, R. L., *et al* (1977) The family history method using diagnostic criteria: reliability and validity. *Archives of General Psychiatry*, **34**, 577–582.

CUTTING, J. (1978) Study of anosognosia. *Journal of Neurology, Neurosurgery and Psychiatry*, **41**, 548–555.

FINKLESTEIN, S., BENOWITZ, L. I., BALDESSARINI, R. J., *et al* (1982) Mood, vegetative disturbance, and dexamethasone suppression test after stroke. *Annals of Neurology*, **12**, 463–468.

FINSET, A. (1988) Depressed mood and reduced emotionality after right hemisphere brain damage. In *Cerebral Hemisphere Function in Depression* (ed. M. Kinsbourne). Washington DC: American Psychiatric Press.

FOLSTEIN, M. F., FOLSTEIN, S. E. & MCHUGH, P. R. (1975) Mini-mental state: a practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, **12**, 189–198.

——, MAIBERGER, R. & MCHUGH, P. R. (1977) Mood disorder as a specific complication of stroke. *Journal of Neurology, Neurosurgery and Psychiatry*, **40**, 1018–1020.

GAINOTTI, G. (1972) Emotional behavior and hemispheric side of the lesion. *Cortex*, **8**, 41–55.

GASPARRINI, W. G., SATZ, P., HEILMAN, K. M., *et al* (1978) Hemispheric asymmetries of affective processing as determined by the Minnesota Multiphasic Personality Inventory. *Journal of Neurology, Neurosurgery and Psychiatry*, **41**, 470–473.

HAMILTON, M. A. (1960) A rating scale for depression. *Journal of Neurology, Neurosurgery and Psychiatry*, **23**, 56–62.

KLEIST, K. (1931) Die storungen der ichleistungen und ihre lokalisation inn orbital-, innen und zwischenhirn. *Monatschrift für Psychiatrie und Neurologie*, **79**, 338–350.

KUNITZ, S. C., GROSS, C. R., HEYMAN, A., *et al* (1984) The pilot Stroke Data Bank: definition, design and data. *Stroke*, **15**, 740–746.

LEVINE, D. N. & GREK, A. (1984) The anatomic basis of delusions after right cerebral infarction. *Neurology*, **34**, 577–582.

LIPSEY, J. R., ROBINSON, R. G., PEARLSON, G. D., *et al* (1983) Mood change following bilateral hemisphere brain injury. *British Journal of Psychiatry*, **143**, 266–273.

NAUTA, W. J. H. (1971) The problem of the frontal lobe: a reinterpretation. *Journal of Psychiatric Research*, **8**, 167–187.

OPPENHEIM, H. (1890) Zur pathologie der grosshirngeschwultse. *Archives für Psychiatrie*, **21**, 560–587.

ROBINSON, R. G. & BENSON, D. F. (1981) Depression in aphasic patients: frequency, severity and clinical pathological correlations. *Brain and Language*, **14**, 282–291.

—— & SZETELA, B. (1981) Mood change following left hemispheric brain injury. *Annals of Neurology*, **9**, 447–453.

——, STARR, L. B., KUBOS, K. L., *et al* (1983) Mood changes in stroke patients: relationship to lesion location. *Comprehensive Psychiatry*, **24**, 555–566.

——, KUBOS, K. L., STARR, L. B., *et al* (1984) Mood disorders in stroke patients: importance of location of lesion. *Brain*, **107**, 81–93.

——, BOLLA-WILSON, K., KAPLAN, E., *et al* (1986) Depression influences intellectual impairment in stroke patients. *British Journal of Psychiatry*, **148**, 541–547.

——, STARKSTEIN, S. E. & PRICE, T. R. (1987) Post-stroke depression and lesion location. *Stroke*, **19**, 125.

ROSS, E. D. & RUSH, A. J. (1981) Diagnosis and neuroanatomical correlates of depression in brain damaged patients. *Archives of General Psychiatry*, **38**, 1344–1354.

RYLANDER, G. (1939) *Personality Changes after Operations of the Frontal Lobes*. London: Oxford University Press.

SINYOR, D., JACQUES, P., KALOUPEK, D. G., *et al* (1986) Post-stroke depression and lesion location: an attempted replication. *Brain*, **109**, 537–546.

STARKSTEIN, S. E., ROBINSON, R. G. & PRICE, T. R. (1987*a*) Comparison of cortical and subcortical lesions in the production of poststroke mood disorders. *Brain*, **110**, 1045–1059.

——, Boston, J. & Robinson, R. G. (1987*b*) Mechanisms of mania following brain injury: twelve case reports and review of the literature. *Journal of Nervous and Mental Disease*, 176, 87–100.

——, Robinson, R. G., Berthier, M. L., *et al* (1988) Depressive disorders following posterior circulation compared with middle cerebral artery infarcts. *Brain*, 111, 375–387.

Starr, L. B., Robinson, R. G. & Price, T. R. (1983) Reliability, validity, and clinical utility of the Social Functioning Exam in the assessment of stroke patients. *Experimental Aging Research*, 9, 101–110.

Wing, J. K., Cooper, J. E. & Sartorius, N. (1974) Measurement and classification of psychiatric symptoms. *Instruction Manual for the PSE*. London: Cambridge University Press.

Zung, W. W. K. (1965) A self-rating depression scale. *Archives of General Psychiatry*, 12, 63–70.

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Cognitive Aspects of Panic Attacks

Content, Course and Relationship to Laboratory Stressors

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Twenty patients with panic attacks and ten controls were given a standardised interview about thoughts occurring during times of anxiety or panic attacks. The interviewer was blind to the subject's diagnosis. The 20 panic patients underwent a psychophysiological test battery which included a cold pressor test, mental arithmetic task, and 5.5% CO_2 inhalation. More patients than controls reported thoughts centred on fears of losing control and shame when anxious. Panic patients rated their thoughts as stronger and clearer than did controls and they had more difficulty excluding them from their minds. A feeling of anxiety preceded anxious thoughts in patients. This suggests that 'faulty cognitions' are not the initial event in a panic attack, although anxious thoughts may exacerbate or maintain them. Significant correlations were found between the intensity of anxiety-related thoughts in anticipation of mental arithmetic and changes in diastolic blood pressure and heart rate during mental arithmetic.

The phenomenology of panic attacks includes physiological, cognitive, and behavioural components. While the physiological and behavioural components of panic have received considerable attention, much less is known about the cognitive component. Recently, researchers have started to apply cognitive theories of anxiety disorders to the study of panic attacks. Beck *et al* (1985) assume that anxiety patients are characterised by "overactive cognitive patterns (schema) relevant to danger that are continually structuring external and/or internal experience as a sign of danger" (Beck *et al*, 1985). Psychophysiological theories posit that panic attacks are the result of a positive feedback loop between bodily symptoms of anxiety and the individual's response to these symptoms (Lader, 1975; Goldstein & Chambless, 1978; Mathews *et al*, 1981; Margraf *et al*, 1986; Clark, 1986; Ehlers *et al*, 1988; Van den Hout, 1988). Internal cues are suggested as triggers for panic attacks. Cognitive processes such as the appraisal of bodily changes or environmental cues perceived as dangerous or as indicating loss of control are considered to be involved in the exacerbation of anxiety. Thus, in this model, a function of cognitions is amplification, leading to higher and higher states of arousal.

The role of cognitions in panic attacks is supported by retrospective interview studies (Beck *et al*, 1974; Hibbert, 1984; Rapee, 1985; Ottaviani & Beck, 1987). Patients with anxiety neurosis reported cognitions related to physical or psychological harm both before and during severe episodes of anxiety (Beck *et al*, 1974). Hibbert (1984) found similar results in 25 out-patients with generalised anxiety or panic disorder. Each of 30 patients with panic disorder interviewed by Ottaviani & Beck (1987) identified ideation centring on themes of physical, mental or behavioural catastrophes. Hibbert (1984) and Rapee (1985) found the cognitions of panic disorder patients during anxiety episodes to be more catastrophic than those of patients with generalised anxiety. In addition, the ideation of panic patients was more centred on internal physical and psychological harm, whereas generalised anxiety patients worried more about social rejection and failure.

Hibbert's study also dealt with the role of physical sensations as anxiety triggers. The most frequently reported sequence of events in panic attacks was the perception of an unpleasant body sensation (e.g., sweaty palms, dsypnoea, or palpitations), followed by anxious catastrophising cognitions and the full-blown picture of a panic attack (Hibbert, 1984). Similarly, Ley (1985) found that somatic symptoms preceded fear in the majority of patients interviewed. Ottaviani & Beck (1987) reported that a misattribution of a physical sensation triggered panic in all their patients.

Since all these studies assessed cognition during panic retrospectively, the data depend on the patients' recollections of their attacks and are susceptible to bias. However, the results are very consistent and thus in line with cognitive or psychophysiological models. Thoughts related to personal danger, therefore, seem to be involved in the exacerbation of anxiety during panic attacks.

The first purpose of our study was to replicate and extend Hibbert's (Hibbert, 1984) investigation of the ideational components of panic. Subjects in Hibbert's study were a mixture of generalised anxiety disorder patients and panic disorder patients with criteria as defined by the Research Diagnostic Criteria (RDC). All patients in the present study met the DSM–III–R criteria for panic disorder (American Psychiatric Association, 1987). We also added a control group.

The second purpose of our study was to analyse the sequence of events of a typical episode of severe anxiety in both patients and control subjects.

Our third purpose was to test the hypothesis that the degree to which panic patients report being disturbed by anxiety-related cognitions is correlated with the degree of physiological arousal in anticipation of, and/or during, a stressful event.

Method

Subjects

Twenty patients suffering from panic attacks were drawn from a treatment study conducted by the Laboratory for the Study of Behavioral Medicine at Stanford University Medical Center and the Laboratory of Clinical Psychopharmacology and Psychophysiology at the Palo Alto Veterans Administration Medical Center. Patients were recruited through advertisements in local newspapers; each was tested for the purposes of the present study during the baseline period of the treatment study prior to any intervention in that study. Sixteen patients were female and four were male. All were Caucasian.

Patients met DSM–III–R criteria for panic disorder with and without agoraphobia as determined by the Structured Clinical Interview for Diagnosis (Spitzer & Williams, 1983; American Psychiatric Association, 1987). Ten patients were diagnosed as having panic disorder and ten as having agoraphobia with panic attacks. Other criteria required that patients be between 18 and 60 years of age, not pregnant, have at least one panic attack per week for the three weeks preceding entrance into the study, and have no active cardiopulmonary, renal, endocrine, or neurological disease. Interviews were conducted by clinicians with special training and experience in the use of the Structured Clinical Interview for Diagnosis (SCID). The age range of the patients was 22–50 years, with a mean age of 34.9 years and a standard deviation of 8.2. The mean score of patients on the Hamilton Anxiety Rating Scale (Hamilton, 1959) was 17.8 ± 8.0.

Ten control subjects were included in the study. These individuals were also recruited through local newspaper advertisements. In order to qualify for the study, controls were required to score at or below the median on both scales of the State-Trait Anxiety Inventory (Spielberger *et al*, 1970). The age range of the controls was 23–52 years, with a mean age of 36.5 ± 11.1 years. All controls were female and Caucasian, and were paid for their participation.

Procedure

Patient and control subjects were interviewed using Hibbert's standardised interview. This instrument has been shown to be reliable and effective in eliciting the most important or troublesome thoughts during times of anxiety (Hibbert, 1984). Patients and controls were interviewed by telephone by one of two interviewers trained in the interview technique. Both interviewers were blind to the diagnostic status of the interviewee.

Interview

Hibbert designed the interview to elicit thoughts which had occurred during times of anxiety during the preceding three weeks. Following introductions and verbal permission to record the conversation, the interviewer said, "I would like you to try to tell me what thoughts have been going through your mind when you have been anxious or something has been making you anxious in the last three weeks". If this question elicited no thoughts, the subject was asked to recall the last time that he or she felt anxious and to describe the situation in detail. Following this description, the subject was asked to recall any thoughts that he or she was having at the time. If this failed to elicit any thoughts, the subject was asked to select a symptom which he or she associated with anxiety and was asked, "What does this symptom/feeling mean to you?" If the reported thoughts were not clearly verbalised, clarification questions were asked. For example, "Can you be more specific about the thought . . . ?" or "Can you tell me what . . . means to you?" were used to clarify any ambiguities. Once a series of thoughts were elicited, the subject was asked to pick the three which seemed most important and to rank these three in order. Subsequently, two independent raters blindly assigned each of these three thoughts to one of seven categories (illness, injury, death, losing control, failure, shame, and other) determined by Hibbert (1984). A satisfactory level of inter-rater reliability was attained (70%). When there was no agreement, the thought was assigned to a category by consensus.

In order to determine the range of thoughts, subjects were asked whether they had had thoughts in the preceding three weeks which fit into six predetermined categories. As Hibbert (1984) points out, these categories are not meant to be 'all inclusive', only to be similar to those indicated by Beck (1974). Next, the quality of the most important thought was determined by asking the subject to rate this thought on an 11-point Lickert scale (0 = 'not at all' and 10 = 'completely' or 'always') with respect to strength, clarity, credibility, frequency, and tenacity.

The subjects were then asked whether or not they had mental images when anxious in the last three weeks and, if so, a series of questions similar to those used for thoughts were asked in order to determine the range and quality of the most important image. The subjects were asked to select from four choices about what happened when they started to get anxious. Similarly, they were asked to select from four choices about what happened when their anxiety began to ease up. Next they were asked to describe briefly what a typical anxiety episode was like for them. Two raters, blind to whether the subject was a patient or a control, independently decided whether a physical sensation, cognition or emotional state occurred first. Inter-rater agreement (agreements divided by agreements plus disagreements) was 83%.

Finally, the subjects were asked to rate the items on the Stanford Panic Appraisal Inventory (SPAI; Telch, 1984). This instrument consists of 20 statements reflecting some common feelings and thoughts that people report at times of fear and anxiety, and is rated using an 11-point Lickert-like scale (0 = 'not at all troubling' and 10 = 'extremely troubling'). The items were selected by asking a group of patients with panic to rank order their five most troublesome concerns with respect to panic from a larger list of possible items. Twenty items were selected which had the highest overall ranking. In an analysis of 100 patients with panic disorder Brouillard (1988) found a Chronbach alpha for internal consistency of 0.90. For test–retest up to ten months $r=0.73$ was obtained. The SPAI is also sensitive to treatment changes (Brouillard, 1988).

The three most important thoughts from the open-ended interview and the three thoughts with the highest scores from the SPAI were used to create a six-statement instrument. This instrument was presented to patients during the physiological testing described below. The statements were listed in random order and rated on an 11-point Lickert scale (0 = 'not at all troubling' and 10 = 'extremely troubling').

Physiological testing

Only patients participated in this portion of the study. In order to minimise interpersonal influences, psychophysiological testing took place in a sound-attenuated, electrically shielded chamber. The patient sat alone and could not see the laboratory personnel during the test periods, but could communicate with them by intercom at any time.

Patients were familiar with the test setting and the assessment procedures since they had undergone a psychophysiological test battery in the same laboratory on the previous afternoon. The cold pressor test and mental arithmetic were presented in balanced order. During the cold pressor test, the patient's dominant foot was immersed in ice water (at 4°C) for one minute. The mental arithmetic task took five minutes and consisted of serial subtractions of 13 starting at 7683 (Ward *et al*, 1983). The recovery periods and the breaks between these two stress tests were sufficient in length to prevent carry-over effects from one stressor to the other. After these 'non-specific' stress tests, subjects were challenged with CO_2 using a single-blind protocol similar to that of Gorman *et al* (1984). Following 15 minutes of room air (placebo), 5.5% CO_2 in room air was given for 20 minutes. The CO_2 inhalation was terminated before 20 minutes if patients reported severe anxiety and asked to stop. Although the patient was blind to the beginning of the CO_2 challenge, he or she was told when it was over. The next 15 minutes was a recovery period in which the patient breathed room air.

Each patient's electrocardiogram was continuously recorded. Heart rate (HR) was calculated from interbeat intervals and was averaged every ten seconds. Systolic (SBP) and diastolic (DBP) blood pressures were measured automatically. For each paradigm, the first blood pressure measurement was taken 60 seconds after the start of the paradigm and then every 4.5 minutes during baseline, every 2 minutes during cold pressor and mental arithmetic tests, and every 2.5 minutes during CO_2 inhalation.

Patients received written instructions prior to each of the three test paradigms (cold pressor, mental arithmetic, and CO_2 challenge). Instructions mentioned the possibility that subjects might feel increases of anxiety with any of the stress tests. After reading the instructions, and in anticipation of the particular test, patients rated the intensity of their three most important interview thoughts and the three thoughts with the highest scores from the SPAI.

Results

Structured interview

The rater-determined categories of the three most important thoughts provided by the patients can be seen in Table I. Patients reported significantly more thoughts focusing on loss of self-control than did control subjects; controls had significantly more thoughts categorised by the raters as 'other'. The subject-determined range of thoughts indicated that patients reported having significantly more thoughts of losing control and shame than did controls (Table II).

TABLE I
Rater-determined categories of three most important interview thoughts

Category	*Patients* (n = *60 thoughts)*		*Controls* (n = *30 thoughts)*	
	%	n	%	n
Illness	18	(11)	13	(4)
Death	7	(4)	0	(0)
Loss of self-control	23	(14)	3	(1)*
Injury to self or other	3	(2)	0	(0)
Inability to cope	12	(7)	17	(5)
Social embarrassment	5	(3)	6	(2)
Other	30	(19)	60	(18)**

$^*P<0.02$, controls v. patients (χ^2 test).
$^{**}P=0.01$.

TABLE II
Patient-determined range of thoughts; percentage of individuals who have thoughts with the designated content when anxious

Category	*Patients* (n = *20)*		*Controls* (n = *10)*		*Hibbert* (n = *17)*	
	%	n	%	n	%	n
Illness	55	(11)	20	(2)**	77	(13)
Death	35	(7)	10	(1)	53	(9)
Losing control	85	(17)	40	(4)*	94	(16)
Injury	45	(9)	50	(5)	12	(2)
Failure	60	(12)	60	(6)	71	(12)
Shame	70	(14)	30	(3)*	47	(8)

$^*P<0.05$, controls v. patients (Fisher's exact test).
$^{**}P<0.08$.

TABLE III
Subjective qualities of 'most important' thought

Subjective qualities	*Patients** (n = *20)*	*Controls** (n = *10)*	P**	*Hibbert patients** (n = *17)*
Strength	8.1	4.5	0.0001	8.0
Clarity	8.9	7.0	0.02	7.8
Ability to exclude from mind when anxious	2.8	6.7	0.0007	3.5
Credibility when anxious	5.8	7.4	NS	3.5
Anxiety present when having this thought	7.9	4.8	0.007	7.3

*Mean Lickert scale (0–10) scores.
**Hotelling T^2-test.

Only two controls reported thoughts centring on illness when they were anxious ($P<0.08$, patients v. controls). Patients in Hibbert's study reported a slightly different pattern from patients in this study, with fewer of them worried about injury during the event and more worried about death.

Table III shows the 'subjective quality' of the most important thoughts for patients and controls. An overall Hotelling T^2-test showed a significant difference between the two groups ($P<0.05$). Subsequent comparisons on single variables revealed that patients were significantly more anxious when having their 'most important thought' than were controls ($t=2.93$, $P=0.007$). In addition, there were significant differences between patients and controls in the subjective quality of the most important thoughts with respect to strength ($t=4.81$, $P=0.0001$), clarity ($t=2.46$, $P=0.02$), and ability to exclude these thoughts from the mind when anxious ($t=3.85$, $P=0.0007$).

When asked during the interview which of four events occurred first during an episode of anxiety, both patients and controls reported that, most frequently, a feeling of anxiety without a thought was the first event of their anxiety (70% for both). Ratings of the patients' and controls' descriptions of a typical anxiety episode corroborated that a feeling of anxiety without a thought was the first reported event, at least in patients. With 83% agreement, two independent raters found that 85% of the patients described a bodily event as the initial occurrence during a typical anxiety episode, while only 44% of controls described a bodily event as the first occurrence.

Presented with four possible sources of relief of anxiety, 40% (8/20) of patients chose 'you fight it and force it out of you', compared with 10% (1/10) of controls ($P<0.1$, Fisher's exact test), while 60% (6/10) of controls chose 'you reassure yourself', compared with 20% (4/20) of patients ($P<0.05$, Fisher's exact test).

Questionnaire

Patients scored significantly higher on the SPAI than controls (85.0 and 26.5, respectively; $t=4.19$, $P=0.0003$).

Physiological correlations

The ratings given by patients to the six thoughts (three interview, three highest scored from SPAI) before exposure to the three stress tests (CO_2 inhalation, cold pressor, mental arithmetic) were correlated with changes in systolic and diastolic blood pressure and changes in heart rate in the anticipation and stress periods. For this purpose, and for each of the stressors' changes, scores were calculated between the sum of the baseline values of these variables and the respective values during anticipation and stress. Correlations using sums of thought ratings yielded the same results as using either individual thoughts or weighted sums of thoughts (i.e. the value given by the patient to the first thought multiplied by three, the value given to the second thought multiplied by 2, and the value given to the third thought multiplied by 1 prior to summing the three thoughts).

The only significant correlation between the sum of anxious thoughts and physiological parameters in *anticipation* of the three stress tests was between the sum of the interview thoughts and the changes in diastolic blood pressure ($r=0.46$, $P<0.05$) in anticipation of mental arithmetic.

Table IV shows correlations between the sums of scores given to the three interview thoughts in anticipation of stress testing and the physiological parameters *during* each of the three stress tests. Significant correlations were obtained between the intensity of thoughts and changes in diastolic blood pressure and heart rate during mental arithmetic.

TABLE IV
Correlations between thought ratings in anticipation of stress testing and changes during stress testing

Sum of intensity scores[1]	*Stress testing variables: change from baseline to task*		
	SBP	*DBP*	*HR*
I-T before CO_2	0.14	0.11	0.15
SPAI-T before CO_2	0.21	0.16	0.24
I-T before MA	0.29	0.38*	0.61**
SPAI-T before MA	0.26	0.49*	0.58**
I-T before CP	0.17	−0.21	0.05
SPAI-T before CP	0.21	−0.10	0.00

*$P<0.05$.
**$P<0.01$.
1. Sum of intensity scores (0–10) of three interview thoughts (I-T) or three Stanford Panic Appraisal Inventory thoughts (SPAI-T) before CO_2, mental arithmetic (MA) or cold pressor (CP). SBP = systolic blood pressure. DBP = diastolic blood pressure. HR = heart rate.

Results were similar for the sum of the three thoughts from the SPAI (also in Table IV).

Discussion

The first purpose of this study was to replicate and extend previous findings on ideation of patients with panic disorder (Hibbert, 1984; Rapee, 1985; Ottaviani & Beck, 1987). We found, in concurrence with Hibbert, that loss of control during times of anxiety is the most common thought in anxious patients.

Of Hibbert's 17 patients with panic attacks, eight reported 'most important thoughts' as having a heart attack (five subjects) or dying (three subjects). In our interview, only one out of 20 reported a thought so directly related to personal danger ('I might have a heart attack') as 'most important'. Further, on the SPAI, the items 'I may have a heart attack' or 'I may die' were endorsed as most important of the 20 items on the scale by only four patients.

This difference might be related to the methodologies of the interviews. Hibbert's (1984) and Beck *et al's* (1974) interviews with patients were conducted face to face; ours were conducted over the telephone. A direct face-to-face interview with a clinician might produce a more anxious state in the subject and thus lead to more thoughts around the issues of personal danger. On the other hand, a telephone interview during which the subject was in familiar and 'safe' surroundings might not predispose the subject to a state of high anxiety and thus might not bias the interview towards eliciting personal danger thoughts. Indeed, several subjects commented that they felt more comfortable revealing details about themselves because the interview was *not* face to face.

The significant differences between patients and controls on the SPAI further support the notion that patients and controls differ in cognitions. Using a cut-off of 50, the SPAI correctly identified 18 anxious patients and 9 controls. Thus, in this population, the SPAI was 90% sensitive and 90% specific.

Although the use of a control group is an improvement over other studies, a control group is subject to the same methodological problems of any self-report study. For both patients and controls, the data are retrospective and subject to recall and experimental demand bias. For instance, non-anxious controls might be reluctant to report a feeling of losing control during anxiety even if they were having one.

The second purpose of this study was to analyse the sequence of events of a typical episode of severe anxiety in both patients and controls. We found that both patients and controls most frequently reported a feeling of anxiety without a thought as the first event in an anxiety episode (70% for both). There were no differences in either of the other three choices by percentage (a thought without a feeling of anxiety, both a thought and feeling at the same time, or don't know). Hibbert found that 53% of his subjects with panic attacks reported a feeling of anxiety without a thought as the first event in an episode of anxiety.

The analysis of the brief descriptions of an episode of anxiety by both patients and controls also supported this finding for patients. In 85% of the patients, a bodily event was the initial awareness of anxiety. It appears that bodily symptoms usually precede other events in anxious patients. This suggests that most of the time 'faulty cognitions' are not the initial event in a panic attack, although they may exacerbate or maintain it.

The third purpose of the present study was to tes the hypothesis that the degree to which panic patients report being disturbed by anxiety-related cognitions is significantly correlated with the degree o physiological arousal in anticipation of and during stressful events. We found that the most importan thought at one time is not necessarily the mos important thought at another. In anticipation of the CO_2 inhalation test, patients did not report the thought that they had indicated during the telephone interview as most troublesome at times of anxiety The same result occurred in anticipation of the cold pressor test. These data suggest that the 'mos important thought' varies from one situation to another, either because thoughts are situationally specific or because an underlying anxious state of mind may predispose to anxious thoughts (Horowitz *et al*, 1983).

Finally, the physiological aspect of this study showed us that the reactivity to physical stressors (cold water and CO_2) did not correlate significantly with an increase in troublesome thoughts either in anticipation of or during these stress tests. The stressors may have produced as yet undefined non stress-related physiological changes which overrode whatever effect cognitions had in producing physiological change. The only significant correlation between change in physiology in response to a stressor and intensity of troublesome thoughts wa found in anticipation of and during the menta arithmetic test. Thus the intensity of cognition wa only significantly related to physiological change in the condition where there was no external stimulus, such as cold water or inhaled CO_2, driving the physiology

The results of our work have several implication for the assessment and treatment of panic disorder First, a paper and pencil test, the SPAI, can be used to differentiate between patients with high anxiety and controls, and presumably would serve as a good outcome measure of changes in cognition in appropriate populations. Second, a focus on security and control issues in the context of therapy might have significant impact on reducing anxiety states which, left to escalate, can and do culminate in panic attacks. These findings are consistent with the cognitive interventions suggested by Beck and Emery (Beck *et al*, 1985) and with the psychophysiological model which suggests that a positive feedback loop, with thoughts as one component of the loop, is responsible for culmination of an anxiety state in a full-blown panic attack. Third, more studies are needed to delineate the phenomenology of anxiety states as they develop over time. Specifically, chronological monitoring of behaviour, physiology, cognition and bodily symptoms might reveal patterns representing discrete panic attacks and anxious states of mind. Further, this kind of monitoring might elucidate whether or not there is a predictable sequence among these anxiety components.

References

American Psychiatric Association (1987) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn, revised) (DSM-III-R). Washington DC: APA.

Beck, A. T., Emery, G. D. & Greenberg, R. (1985) *Anxiety Disorders and Phobias, a Cognitive Perspective*. New York: Basic Books.

——, Laude, R. & Bohnert, M. (1974) Ideational components of anxiety neurosis. *Archives of General Psychiatry*, **31**, 319–325.

Brouillard, M. (1988) Effects of behavioral, cognitive behavioral, and drug treatments on the catastrophic fears of agoraphobics. Unpublished dissertation, Stanford University.

Clark, D. M. (1986) A cognitive model of panic. *Behaviour Research and Therapy*, **24**, 461–470.

Ehlers, A., Margraf, J. & Roth, W. T. (1988*a*) Interaction of expectancy effects and stressors in a laboratory model of panic. In *Neurobiological Approaches to Human Disease* (eds D. Hellhammer, I. Florin & H. Weiner). Toronto: Huber.

——, Margraf, J. & Roth, W. T. (1988*b*) Selective information processing, interoception, and panic attacks. In *Treatment of Panic and Phobias* (eds I. Hand & H. U. Wittchen). Berlin: Springer.

Goldstein, A. J. & Chambless, D. L. (1978) A reanalysis of agoraphobia. *Behavior Therapy*, **9**, 47–59.

Gorman, J., Askanazi, J., Liebowitz, M., *et al* (1984) Response to hyperventilation in a group of patients with panic disorder. *American Journal of Psychiatry*, **141**, 857–861.

Hamilton, M. (1959) The assessment of anxiety state by ratings. *British Journal of Medical Psychology*, **32**, 50–55.

Hibbert, G. A. (1984) Ideational components of anxiety. *British Journal of Psychiatry*, **144**, 618–624.

Horowitz, M. J., Simon, N., Holden, M., *et al* (1983) The stressful impact of news of risk for premature heart disease. *Psychosomatic Medicine*, **45**, 32–40.

Lader, M. (1975) *The Psychophysiology of Mental Illness*. London: Routledge and Kegan Paul.

Ley, R. (1985) Agoraphobia, the panic attack and hyperventilation syndrome. *Behaviour Research and Therapy*, **23**, 79–81.

Margraf, J., Ehlers, A. & Roth, W. T. (1986) Biological models of panic disorder and agoraphobia: a review. *Behaviour Research and Therapy*, **24**, 553–567.

Mathews, A. M., Gelder, M. G. & Johnston, D. W. (1981) *Agoraphobia: Nature and Treatment*. New York: Guilford Press.

Ottaviani, R. & Beck, S. T. (1987) Cognitive aspects of panic disorders. *Journal of Anxiety Disorders*, **1**, 15–28.

Rapee, R. (1985) Distinction between panic disorder and generalized anxiety disorder: clinical presentation. *Australian and New Zealand Journal of Psychiatry*, **19**, 227–232.

Spielberger, C. D., Gorsuch, R. L. & Lushene, R. E. (1970) *State–Trait Anxiety Inventory*. Palo Alto: Consulting Psychologists Press.

Spitzer, R. L. & Williams, J. B. (1983) *Structured Clinical Interview for DSM-III*. New York: New York State Psychiatric Institute.

Telch, M. J. (1984) Stanford Panic Appraisal Inventory. Unpublished scale, Stanford University.

Van den Hout, M. A. (1988) The explanation of experimental panic. In *Panic: Psychological Perspectives* (eds S. Rachman & J. D. Maser). Hillsdale, N. J.: Lawrence Erlbaum.

Ward, M. M., Mefford, I. N., Parker, D., *et al* (1983) Epinephrine and norepinephrine responses in continuously collected human plasma to a series of stressors. *Psychosomatic Medicine*, **45**, 471–486.

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Point of View

Concordance by Sex in Sibling Pairs with Schizophrenia is Paternally Inherited

Evidence for a Pseudoautosomal Locus

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The hypothesis that the gene for schizophrenia is located in the pseudoautosomal region of the sex chromosomes predicts that same-sex concordance will occur in paternally rather than maternally derived pairs. In 120 families that included at least one sibling pair with schizophrenia, affected members were significantly more likely to be of the same sex when there was a history of illness on the paternal than on the maternal side, the difference remaining significant when parent of origin was assessed by three different methods. The finding is as predicted by the pseudoautosomal hypothesis: therefore a search for the gene should be focused on this small (three megabase) region of the genome. The ratio of same to mixed sex pairs in paternally-derived cases (approximately 3 : 1) suggests the gene is located in the centromeric one-third of the pseudoautosomal region.

A role for genes in the aetiology of schizophrenia is supported by twin and adoption studies (Gottesman & Shields, 1982), but neither the genomic locus nor the mode of inheritance has been identified. A locus on the sex chromosomes has not been widely entertained. Although sex linkage has been considered (e.g. by Slater, 1953*b*) for occasional pedigrees, a sex chromosomal locus for schizophrenia in general appears to be ruled out by approximately equal incidence in the two sexes and equal risk to the children of affected men and affected women. However, gender does influence the pattern of psychosis within families. Mott (1910) was the first to report a tendency for pairs of relatives with psychosis to be more frequently of the same than of mixed sex. The phenomenon was also noted by Myerson (1925) and Penrose (1942). Table I summarises published studies of psychotic sibling pairs; a 28% excess of same-sex pairs is present.

Sturt & Shur (1985) have drawn attention to various types of sampling bias, particularly those associated with incomplete or biased ascertainment, that might account for same-sex concordance. But such concordance is also seen in dizygotic twin pairs; in this case some of the ascertainment biases described by Sturt & Shur are not relevant and sampling errors can be checked by a comparison with same : mixed sex ratios in discordant pairs (Table II). A substantial same-sex excess in concordant pairs is still present.

It was previously suggested (Crow, 1983) that contagion might be a factor in the aetiology of schizophrenia, and that same-sex concordance could reflect an environmental influence, for example related to closer proximity of same-sex by comparison

TABLE I
Distribution by sex in sibling pairs with schizophrenia

	Schulz (1932)	*von Zehnder* (1941)	*Penrose* (1945)	*Tsuang* (1967)	*Totals*
Same sex	75	43	230	19	367
Mixed sex	56	29	192	9	286

Sign test (for the comparison with a 50 : 50 distribution) $z = 3.13$, $P < 0.001$.

TABLE II
Concordance for schizophrenia by sex in dizygotic twin pairs

	Slater (1953a)		*Rosanoff* et al *(1934/35)*		*Kallmann (1946)*		*Kringlen (1968)*		*Totals*	
	conc.	*disc.*	*conc.*	*disc.*	*conc.*	*disc.*	*conc.*	*disc.*	*conc.*	*disc.*
Same sex	11	50	10	43	34	262	6	84	61	439
Mixed sex	2	52	5	43	13	208	8	74	28	377

Same : mixed sex ratio = 2.17 (concordant), 1.16 (discordant). conc. = concordant; disc. = discordant. Sign test (for the comparison with a 50 : 50 distribution) $z = 3.8$, $P < 0.0002$.

with opposite-sex siblings. But analysis of age of onset of psychosis in siblings ruled out contagion and other post-natal environmental influences (Crow & Done, 1986). Therefore if concordance by sex is not an artefact and cannot be attributed to the environment, it may have a genetic explanation. Given the apparent absence of sex linkage, Penrose (1942) considered an influence of auxiliary (i.e. autosomal) genes for determining sex. An alternative explanation (Crow, 1987, 1988) is that the psychosis locus is in the pseudoautosomal region (Fig. 1).

In male meiosis a single obligatory crossing over takes place in a small segment of the distal short arms of the X and Y chromosomes (Burgoyne, 1986). Within this region homology of sequence between X and Y chromosomes is present (Goodfellow *et al*, 1983), and there is a gradient of sex linkage from the sex-chromosome-specific region out to the short-arm telomere (Rouyer *et al*, 1986). Genes within the region are transmitted in a manner that appears autosomal but has one additional characteristic. If a father carries a defective gene in this part of his X chromosome he is likely to have affected daughters, but if he carries the gene on the corresponding part of the Y chromosome his sons are at greater risk. Therefore affected individuals will be more often of the same sex than the 50:50 expectation. If the gene is at the telomere (where 50% recombination takes place), or when transmission is from the mother, no such effect is predicted. On account of the gradient of sex linkage the size of the concordance effect gives a clue to the location of the gene within this region.

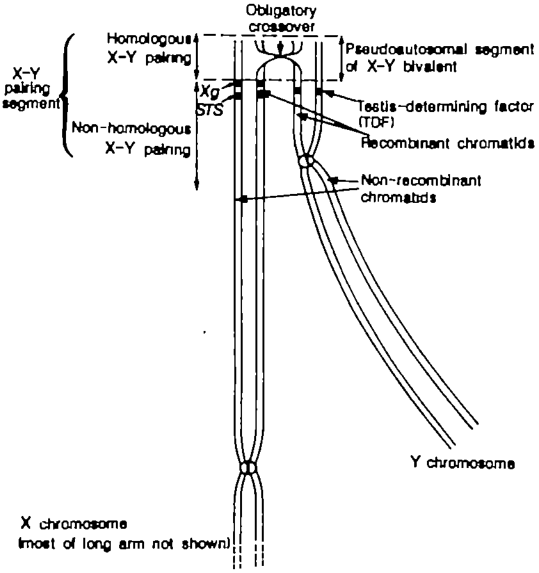
Obligatory crossover
Homologous X-Y pairing
X-Y pairing segment
Non-homologous X-Y pairing
Xg
STS
Pseudoautosomal segment of X-Y bivalent
Testis-determining factor (TDF)
Recombinant chromatids
Non-recombinant chromatids
Y chromosome
X chromosome (most of long arm not shown)

FIG. 1 Crossing over between X and Y chromosomes in male meiosis in the human pseudoautosomal region. Within this segment there is homology of genetic sequence between X and Y chromosomes. In male meiosis a single obligatory crossing over takes place as indicated: since this cross-over occurs within a confined region, recombination here is high relative to that within the region in female meiosis and in the rest of the genome. Because the position of the cross-over varies, a gradient of sex linkage exists within the region such that for genes located at the telomere (where there is 50% recombination) sex linkage is absent. By contrast, sex linkage (and concordance by sex) is greatest for genes located close to the pseudoautosomal limit. X_g = location of X_g blood group gene; *STS* = steroid sulphatase gene. (Reproduced by permission from Burgoyne (1986). Copyright ©1986 Macmillan Magazines Ltd.)

Method

We examined concordance by sex in two series of pairs of siblings with schizophrenia: (a) a series (79 sibships from 78 families) collected (from January 1985 to September 1988) across the United States with the help of the National Alliance for the Mentally Ill (NAMI) under the auspices of the Clinical Neurogenetics Branch of the National Institute of Mental Health and at the State University of New York at Stonybrook; and (b) a population-based series (41 families) collected under the auspices of the UK Medical Research Council at a district general hospital (Northwick Park Hospital; NPH) in north-west London.

Criteria for inclusion were (a) that each individual had suffered from a psychotic illness of sufficient severity to require hospital admission, and (b) that the illness met the criteria for a diagnosis of chronic schizophrenia or schizoaffective disorder by Research Diagnostic Criteria (RDC) (series 1) or fulfilled the St Louis criteria for schizophrenia, or on Present State Examination were placed in one of the CATEGO schizophrenic categories (series 2). Clinical features of 53 sets of siblings from the first series have been previously reported (DeLisi *et al*, 1987). A brief report of concordance by sex in the combined series has also appeared (Crow *et al*, 1989) without the detailed classification of family history employed here or the statistical correction in pairwise analysis discussed below.

In each series an attempt was made to identify other family members with major psychiatric illness by interview with multiple informants. Families were classified according to whether there was a history of illness on the maternal or paternal sides, by means of three alternative systems of classification:

(a) a 'hierarchical' system in which the parental origin of illness was designated according to the following order of priorities:
   (i) *schizophrenia* in a parent
   (ii) schizophrenia in a first-degree relative of a parent
   (iii) schizophrenia a second-degree relative of a parent
   (iv) *psychosis not otherwise specified* (NOS) in a parent
   (v) psychosis NOS in a first-degree relative of a parent
   (vi) psychosis NOS in a second-degree relative of a parent
   (vii) *affective disorder* in a parent
   (viii) affective disorder in a first-degree relative of a parent.

In this system one step in the diagnostic sequence from schizophrenia through psychosis NOS to affective disorder was considered equivalent to one step in the sequence from parent to first- and second-degree relative of parent. Thus affective disorder in a parent, psychosis NOS in a first-degree relative, and schizophrenia in a second-degree relative of a parent were considered equivalent. Thus if affective disorder was present in the mother and psychosis NOS in the father's brother, the family was designated bilateral.

(b) a 'unilateral' system in which parental origin was designated when illness (as defined in any of the above categories) was present on one but not on the other side

(c) a 'closest relative' system in which parental origin was designated by the relative closest in the chain, from parent to first-degree and then second-degree relative of a parent, to be affected by any of the above categories of illness.

In each case some families were classified as having illness on both or on neither parental sides (Tables III and IV). Classification by the 'unilateral' system minimises the number of families that are allocated to either paternal or maternal categories and maximises those in the 'both' category, while the 'closest relative' system has the opposite effect. The 'hierarchical' system can be used to examine the influence of particular illnesses (e.g. schizophrenia or affective illness) in preceding generations (Table VI), and the relationship of the affected individual (Table VII), on the pattern of inheritance in the sibling pairs.

Figure 2 illustrates the way in which the three methods of classification are applied in a pedigree that is allocated to a different category by each method.

In a number of sibships more than two individuals were affected. Analysis by sex was carried out both sibshipwise (i.e. by determining whether or not all affected individuals in a sibship were of the same sex) and pairwise (assessing individual pairs within each sibship). The latter provides more information by taking into account the fact that each meiosis is an independent event. However, it is necessary to correct for the fact that there are not as many independent events (i.e. births of a sibling) as the total of all possible pairs within a sibship. A 'weighted-pairs' correction (Suarez & van Eerdewegh, 1984) was therefore applied. In these families each individual pairing was multiplied by a factor of $2/n$ where n is the number of affected members. Thus in a family with four ill siblings there are six possible pairs but each of these pairs is given a value of 2/4 (i.e. ½).

Results

The sex distribution and classification of family histories by the three systems is given in Table III. Both series include a number of sibships with more than two affected members, in three cases with four, and one with six affected individuals.

A noteworthy finding is that even with the classifications that maximise usage of family history information, a high proportion of families (at least 24% in the NAMI series and over 40% in the NPH series) have no relatives beyond those in the sibship itself with recognised psychiatric disorder. The distribution by sex of these pairs in the two series is different – 10 : 8 : 1 mm : mf : ff in the NAMI series and 2 : 9 : 7 in the NPH series, according to the 'closest relative' classification.

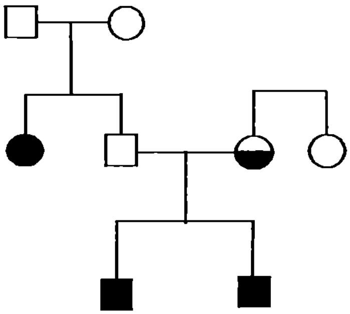

FIG. 2 A pedigree to illustrate the method of classifying sibships with respect to parental origin of illness. In this family parental origin is classified differently by each of the three systems – by the 'hierarchical' system it is paternal because schizophrenia in a first-degree relative of a parent takes precedence over affective illness in a parent; by the 'unilateral' system it is 'both', because there is illness on both paternal and maternal sides; and by the 'closest relative' system the sibship is classified as maternal on account of the depressive illness of the mother. (□ male, ○ female; ■● schizophrenia, ◒ unipolar depression.)

Allocation of sibships to the categories 'paternal', 'maternal', 'both' and 'neither' (Table IV) indicates that with each of the three systems of classification there is an excess of same-sex over mixed-sex pairs in the paternally derived sibships. The excess (15 : 5) is greatest with the 'unilateral' system. The ratio of same-sex to mixed-sex pairings is significantly greater in paternally than maternally derived pairs ($P < 0.008$ to $P < 0.02$, Fisher's exact test).

The excess of same-sex pairs in the paternally derived sibships is independent of the method of classification of family history. However, there is an excess of males in the series (167 : 100) that relates particularly to the NAMI cases (127 : 51) but is absent from the NPH sample (40 : 49). Presumably it arises from the method of collection by recruitment through a mailed newsletter to the NAMI membership. Perhaps this elicited a response that included an excess of more seriously affected individuals who are likely to be of earlier onset and male. Such an excess could explain an excess of same-sex (male) over mixed-sex pairs, but it cannot account for the difference in same : mixed sex ratios in the maternally and paternally derived pairs, particularly the deficit of mixed sex pairs among the latter.

Each sibship including more than two affected individuals carries more information than has been used in the above analysis. To obtain as accurate as possible an estimate of the size of the concordance-by-sex effect, a pairwise analysis was conducted with the weighted-pairs correction.

The analysis (Table V) indicates that whereas the ratio of same-sex to mixed-sex pairs in the maternally derived sibships is less than but approaching unity, the ratio in the paternally derived sibships is consistently greater (2.4–3.5). As in the sibship analysis (Table IV), the paternal excess is relatively insensitive to the method of designating parental derivation.

TABLE III

Distribution by sex of affected individuals in relation to parental derivation of illness according to three classifications of family history

	Hierarchical				*Unilateral*				*Closest relative*				*Totals*
	pat.	*mat.*	*both*	*none*	*pat.*	*mat.*	*both*	*none*	*pat.*	*mat.*	*both*	*none*	
NAMI series (total no. of sibships, 79; total no. of individuals, 178)													
2m	8	8	4	13	8	8	7	10	10	10	3	10	33
2f	2		3	1	1		4	1	3	1	1	1	6
mf	3	10	5	8	2	9	7	8	5	12	3	6	26
2m, 1f	1	1	1	2	1	1	2	1	2	1	1	1	5
1m, 2f		2				2				2			2
3m	1		1		1		1		1	1			2
3f		1				1				1			1
3m, 1f				1				1				1	1
4m	1		1		1		1		2				2
6m	1						1		1				1
Totals	17	22	15	25	14	21	23	21	24	28	8	19	
All male	11	8	6	13	10	8	10	10	14	11	3	10	
Mixed sex	4	13	6	11	3	12	9	10	7	15	4	8	
All female	2	1	3	1	1	1	4	1	3	2	1	1	
NPH series (total no. of sibships, 41; total no. of individuals, 89)													
2m	2	1	1	1	2	1	1	1	2	1	1	1	5
2f	2	2	1	7	2	2	1	7	3	2		7	12
mf	3	6		8	2	5	2	8	4	6		7	17
2m, 1f		3		1		2	1	1		3		1	4
1m, 2f		1		1		1		1		1		1	2
3m				1				1				1	1
Totals	7	13	2	19	6	11	5	19	9	13	1	18	
All male	2	1	1	2	2	1	1	2	2	1	1	2	
Mixed sex	3	10		10	2	8	3	10	4	10		9	
All female	2	2	1	7	2	2	1	7	3	2		7	
Totals for both series (total no. of sibships, 120)													
All male	13	9	7	15	12	9	11	12	16	12	4	12	
Mixed sex	7	23	6	21	5	20	12	20	11	25	4	17	
All female	4	3	4	8	3	3	5	8	6	4	1	8	

pat., paternal; mat., maternal; m, male; f, female.

TABLE IV

Concordance by sex in sibships with schizophrenia classified by family history according to three systems

Classificatory system	*Paternal*	*Maternal*	*Both*	*Neither*	*Totals*
'Hierarchical'[1]					
same sex	17	12	11	23	63
mixed sex	7	23	6	21	57
'Unilateral'[2]					
same sex	15	12	16	20	63
mixed sex	5	20	12	20	57
'Closest relative'[3]					
same sex	22	16	5	20	63
mixed sex	11	25	4	17	57

1. $P=0.008$; 2. $P=0.01$; 3. $P=0.02$. All values by Fisher's exact two-tailed *t*-test. For comparison of maternally v. paternally derived sibships.

TABLE V
Pairwise analysis of concordance by sex using a weighted-pairs correction

	Hierarchical		*Unilateral*		*Closest relative*	
	Paternal	*Maternal*	*Paternal*	*Maternal*	*Paternal*	*Maternal*
Same sex	24.66	17.66	18.66	17	31	22.66
Mixed sex	7.33	25.33	5.33	22	13	27.33
Same : mixed Sex ratio	3.36	0.69	3.50	0.77	2.38	0.83
Fisher's exact *P* (two-tailed)	0.002		0.009		0.02	

Hierarchical analysis allows the influence of type of psychiatric illness (Table VI) and proximity of affected individual in preceding generations (Table VII) to be assessed.

In each case the numbers are small. They suggest that paternal transmission of concordance by sex is at least as pronounced when there is a diagnosis of schizophrenia in the preceding generations as when parental origin is determined on the basis of other diagnoses (Table VI), and that the effect is relatively independent of the relationship of the individual on whose illness parental origin is assigned (Table VII).

Discussion

The finding that siblings who have inherited psychotic illness from their father are more often of the same sex than those inheriting illness from the mother is what would be expected if the gene were located within the pseudoautosomal region. Other explanations for same-sex concordance (e.g. that it results from shared psychological environment (Rosenthal, 1962) or 'auxiliary' sex-determining genes (Penrose, 1942)) have been offered but would not have predicted dependence upon paternal rather than maternal inheritance. The excess of males in the NAMI series could lead to concordance by sex in the series as a whole, as pointed out by Sturt & Shur (1985), but it cannot explain the relevance of the sex of the transmitting parent. One possibility, compatible with observations in the literature (Crow, 1988), is that in some cases the disease is preferentially transmitted from father to son. Such transmission suggests a locus on the Y chromosome, but this is consistent with equal incidence in the two sexes in general only if the gene is within the pseudoautosomal region.

Underlying the above analysis is the assumption that the mode of transmission is dominant, that is the gene originates either on the paternal or the maternal side. However, in a surprising proportion of families (31% overall) no cases of psychiatric illness were detected outside the sibship. Had the sibships been smaller and included only one affected member, the case might well have been described as 'sporadic' and therefore non-genetic (Goldin *et al*, 1987), or attributed to new mutation. This would have been an error – on the contrary, the distribution in these families is consistent with recessive transmission. Such a mode of transmission for schizophrenia was previously proposed, for example by Kallmann (1946). However, not infrequent occurrence in parent–child pairs (see e.g. Penrose, 1968) suggests a dominant gene.

TABLE VI
Concordance by sex in relation to type of illness in parent or parental relative

Diagnosis in relative	*Parental origin*	
	Paternal	*Maternal*
Schizophrenia		
same sex	8	3
mixed sex	1	11
Psychosis NOS		
same sex	6	4
mixed sex	5	6
Affective disorder		
same sex	4	5
mixed sex	1	5

TABLE VII
Concordance by sex in relation to proximity of illness in parents and their relatives

Affected relative	*Parental origin*	
	Paternal	*Maternal*
Parent		
same sex	6	6
mixed sex	3	12
First-degree relative of parent		
same sex	7	5
mixed sex	3	9
Second-degree relative of parent		
same sex	5	1
mixed sex	1	1

Book (1953) and Slater (1958) postulated an 'intermediate' mode of transmission, that is, manifestation in all homozygotes (recessive) but in only a proportion of heterozygotes (dominant transmission). The present findings are consistent with such a concept but its molecular meaning is obscure.

Since there is a gradient of sex linkage within the pseudoautosomal region (Rouyer *et al*, 1986) the ratio of same to mixed sex in the paternally derived pairs gives an indication of the location of the gene within this region. Concordance by sex will be maximal (i.e. paternally/derived pairs of siblings will always be of the same sex) with a gene at the boundary of the pseudoautosomal region (i.e. closest to the centromere) whereas at the telomere, where there is 50% recombination in male meiosis, concordance by sex will be absent. The numbers are small but the ratio (2.4–3.5 : 1, Table V) suggests a location relatively low within this segment, perhaps in the centromeric one-third. It should be noted that if there is heterogeneity, that is if some cases of schizophrenia are linked to loci elsewhere, or if there are errors in designating parental origin of illness, this will reduce the ratio. Therefore the gene may be close to the pseudoautosomal limit.

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References

Book, J. A. (1953) A genetic and neuropsychiatric investigation of a North Swedish population, with special regard to schizophrenia and mental deficiency. *Acta Genetica (Basel)*, 4, 1–100, and 345–414.

Burgoyne, P. S. (1986) Mammalian X and Y crossover. *Nature*, 319, 258–259.

Crow, T. J. (1983) Is schizophrenia an infectious disease? *Lancet*, *i*, 173–175.

—— (1987) Pseudoautosomal locus for psychosis? *Lancet*, *ii*, 1532.

—— (1988) Sex chromosomes and psychosis: the case for a pseudoautosomal locus. *British Journal of Psychiatry*, 153, 675–683.

—— & Done, D. J. (1986) Age of onset in schizophrenia: a test of the contagion hypothesis. *Psychiatry Research*, 18, 107–117.

——, DeLisi, L. E. & Johnstone, E. C. (1989) Clues to the nature and location of the psychosis gene: is schizophrenia due to an anomaly of the cerebral dominance gene located in the pseudoautosomal region of the sex chromosomes? In *Genetics of Neuropsychiatric Disease*, Proceedings of a conference held from 26 to 28 May 1988 at the Wenner-Gren Center, Stockholm (ed. L. Wetterberg). Basingstoke: Macmillan.

DeLisi, L. E., Goldin, L. R., Maxwell, E., *et al* (1987) Clinical features of illness in siblings with schizophrenia or schizo-affective disorder. *Archives of General Psychiatry*, 44, 891–896.

Goldin, L. R., DeLisi, L. E. & Gershon, E. S. (1987) Unravelling the relationship between genetic and environmental risk factors in psychiatric disorders. *British Journal of Psychiatry*, 151, 302–305.

Goodfellow, P., Banting, G., Sheer, D., *et al* (1983) Genetic evidence that a Y-linked gene in man is homologous to a gene on the X chromosome. *Nature*, 302, 346–349.

Gottesman, I. I. & Shields, J. (1982) *Schizophrenia: The Epigenetic Puzzle*. Cambridge: Cambridge University Press.

Kallman, F. J. (1946) The genetic theory of schizophrenia: an analysis of 691 schizophrenic twin index families. *American Journal of Psychiatry*, 103, 309–322.

Kringlen, E. (1968) *Heredity and Environment in the Functional Psychoses: an Epidemiological-Clinical Twin Study*. London: Heinemann.

Mott, F. W. (1910) Hereditary aspects of nervous and mental diseases. *British Medical Journal*, *ii*, 1013–1020.

Myerson, A. (1925) *Inheritance of Mental Disease*. Baltimore: Williams & Wilkins.

Penrose, L. S. (1942) Auxiliary genes for determining sex as contributory causes of mental illness. *Journal of Mental Science*, 88, 308–316.

—— (1945) Survey of cases of familial mental illness. Mimeographed document prepared for the Division of Psychiatric Research, Ontario Department of Health, abstracted in *Digest of Neurology & Psychiatry*, 13, 644.

—— (1968) Critical survey of schizophrenia genetics. In *Modern Perspectives in World Psychiatry* (ed J. G. Howells) pp 3–19. Edinburgh: Oliver & Boyd.

Rosanoff, A. J., Handy, L. M., Plesset, I. R., *et al* (1934/35) The etiology of so-called schizophrenic psychoses. *American Journal of Psychiatry*, 91, 247–286.

Rosenthal, D. (1962) Familial concordance by sex with respect to schizophrenia. *Psychological Bulletin*, 59, 401–421.

Rouyer, F., Simmler, M-C., Johnsson, C., *et al* (1986) A gradient of sex linkage in the pseudoautosomal region of the human sex chromosomes. *Nature*, 319, 291–295.

Schulz, B. (1932) Zur Erbpathologie der Schizophrenie. *Zeitschrift für die Gesammte Neurologie und Psychiatrie*, 143, 175–293.

Slater, E. T. O. (1953*a*) *Psychotic and Neurotic Illness in Twins*. London: HMSO.

—— (1953*b*) Sex-linked recessives in mental illness? *Acta Genetica et Statistica Medica*, 4, 273–280.

—— (1958) The monogenic theory of schizophrenia. *Acta Genetica (Basel)*, 8, 50–56.

Sturt, E. & Shur, E. (1985) Sex concordance for schizophrenia in proband-relative pairs. *British Journal of Psychiatry*, 147, 44–47.

Suarez, B. K. & van Eerdewegh, P. (1984) A comparison of three affected sib-pair scoring methods to detect HLA-linked disease susceptibility genes. *American Journal of Medical Genetics*, 18, 135–146.

Tsuang, M. T. (1967) A study of pairs of siblings both hospitalised for mental disorder. *British Journal of Psychiatry*, 113, 283–300.

von Zehnder, M. (1941) Uber Krankheitsbild und Krankheitsverlauf bei schizophrenen Geschwistern. *Monatschrift fur Psychiatrie und Neurologie*, 103, 231–277.

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Liaison Psychiatry in a Breast Cancer Unit

CHRISTINE DEAN and PENELOPE HOPWOOD

"The first 50 referrals to a newly established liaison psychiatry service for the breast cancer unit at Guy's Hospital, London, have been examined. The majority of referrals were for psychological reactions to malignant disease; most of these were mood disturbances. Patients with sustained psychological reactions to their malignant disease were more likely to have had treatment for previous psychiatric illness and to lack a confiding relationship compared with those whose psychological reactions were transient. Teaching doctors and nurses to deal effectively with the transient psychological reactions of patients to their malignant disease is an important task of liaison psychiatry."

The summary quoted above is from an article by Ramirez (1989). The present authors were invited to comment upon the study.

Christine Dean

It is interesting to note that after several decades of research in this area, only 1.7% of breast cancer patients were referred to the new liaison service described in this study; there is considerable agreement that in the first two years following mastectomy and in patients with advanced breast cancer, 25% of women have an affective illness. The low referral rate may be because the illnesses are not very severe, and indeed the liaison psychiatrist in this study considered that only half of the referred women had an illness. Unfortunately, we do not know what factors actually determined referral, because there are no data on the base population of 3000 women.

The psychological morbidity of mastectomy was first described by Renneker & Cutler (1952). In my own research (Dean, 1987), most of the illnesses following mastectomy were found to be minor affective illnesses; a year after mastectomy, only 5% had an illness which a psychiatrist would regard as severe enough to require treatment. Many of the women did not regard themselves as ill and were not keen to be referred to a psychiatrist. Distinguishing between normal distress and illness can be quite difficult – a problem which is also encountered following bereavement, and which does not seem to have been very satisfactorily resolved in the Ramirez study. It would seem undesirable for 25% of women who have breast cancer to be referred to a psychiatrist, thereby adding the stigma of being a psychiatric patient to their already distressing circumstances. The use of a nurse counsellor and referral to a general practitioner would be a much better option in the majority of cases.

It could be thought that the recent moves to treat early cancers with breast conservation rather than mastectomy might remove the need for a counselling service. However, preliminary findings (Fallowfield *et al*, 1986) indicate that women whose breasts are conserved have rates of morbidity as high as women who have a mastectomy; the diagnosis rather than the treatment seems to be the main cause of distress.

As well as the desire to improve the quality of life of cancer patients by treating their psychiatric morbidity, there is recent interest in the fact that psychological factors may play a role in recurrence and death in breast cancer patients. The most influential study in the field of breast cancer is that by Greer's group (Greer *et al*, 1979; Pettingale *et al*, 1985). In an unselected series of 57 women with early breast cancer, they found that those who were coping at three months after operation with an attitude of fighting spirit or denial had a better chance of disease-free survival than those coping with a strategy of hopelessness or helplessness and stoic acceptance. I have myself just completed a study of an unselected series of 127 women with early breast cancer, which found that women who showed much distress before operation and those who coped with an attitude of denial three months after operation both had a greater chance of disease-free survival. This was after physical determinants of outcome, such as histological node status, tumour size, and treatment of the cancer had been taken into account. There have also been studies which have included patients at all stages of the disease. Jensen (1987) found that poor prognosis was associated with reduced expression of negative affect and with an attitude of helplessness and hopelessness; staging at initial diagnosis was controlled for in this study. Hislop *et al* (1987), in a well designed study of 127 patients with breast cancer, found that high extraversion, low anger, and high levels of social contact at home were all related to better survival. On the whole, studies of patients with advanced breast cancer (Cassileth *et al*, 1985; Holland *et al*, 1986) have found no relationship between psychological factors and survival.

Taking the evidence so far, there does seem to be some support for the view that psychological factors can influence recurrence and survival, particularly in early breast cancer. The consensus appears to be that short-lived distress and expression of negative emotions at the time of diagnosis are associated with a good prognosis, while prolonged apathy and helplessness and hopelessness are associated with a bad prognosis. After the initial adjustment to the cancer, an attitude of fighting spirit or denial is associated with a good prognosis, as is good social support. It is possible that such support facilitates the expression of distress and results in its resolution, producing a more positive response to the cancer and to the resumption of a normal lifestyle. The paper by Dr Ramirez confirms that the patients with a prolonged psychiatric illness were less likely to have a confiding relationship.

There are a few immunological studies which have examined the association between psychological factors and immunological parameters, as this is one way in which psychological factors may be mediated. Levy *et al* (1985) found that when women were assessed within one week of mastectomy, those who were more distressed and maladjusted had higher natural killer cell (NK) activity, and that high NK activity was associated with good outcome in patients with breast cancer. Pettingale *et al* (1981) found that women who were coping with a strategy of denial three months after operation had higher IgM activity than those responding with fighting spirit or stoic acceptance. The group with fighting spirit had significantly lower levels of IgG than those who showed stoic acceptance. They speculate that psychological responses could influence the patient's immune response by increasing non-complement-fixing antibodies (including IgG2 and IgG4), which could act as blocking factors and prevent the destruction of tumour cells or enhance the production of strongly complement-fixing antibodies (of which IgM is one), which would increase destruction of tumour cells.

This area of study is as yet in its infancy, but if studies continue to confirm the contribution of psychological factors to outcome, then the role of psychiatric liaison services and counselling will become an important part of the treatment of breast cancers and probably other cancers as well. On the basis of current evidence, it would be necessary to have a counselling service which would allow the patients to express their current distress, would help the patient to marshal good social support, and would refer for psychiatric treatment patients who had persistent apathy, hopelessness, and helplessness.

Penelope Hopwood

Dr Ramirez draws our attention to many important issues in her review of this clinical liaison service. However, she acknowledges one weakness in her paper – the lack of clarity or precision over the definition of psychiatric illness. Although this may seem a glaring fault, I can sympathise with the author because she is reflecting the state of the art in this field. To date, several different criteria have been used to describe psychological morbidity even in well designed, carefully conducted research studies (Morris *et al*, 1977; Devlen *et al*, 1987; Dean, 1987), so where does the pragmatic psychiatrist set the threshold? It may be straightforward to discriminate 'case' depression, but less easy to set the lower limit for 'borderline' depression, particularly when distress is deemed understandable.

A problem in using the 'distress' and 'illness' categories, as described in this paper, is that it is unclear how certain the classification is at the time of assessment, since length/mode of intervention is used to describe it. A firmer basis, including symptom profile, duration of symptoms, and interference with normal function, would need to be applied to any intervention study in these groups of patients.

Dr Ramirez suggests that many of the patients who were referred close in time to receiving bad news had unmet needs. While this may be true, it may also reflect the nature of the referral pattern, since it is possible that medical and nursing staff are more aware of the likelihood of distress in this context, and more likely to pass the buck. She omits to examine the relevance of the quality of doctor–patient communication in this context – an area we know little about. The theory that sensitive, clear communication, delivered with support from the professionals, would result in less distress on behalf of the recipient warrants testing. She is right to consider directing her training skills to the carers who could then deal with this distress, but it is also possible that some transient reactions will resolve without intervention, and research is badly needed to clarify this question. Vulnerability to psychiatric illness, mild or marked, is also an area to which Dr Ramirez correctly draws our attention, and it is interesting that predictive factors begin to emerge, even with these small numbers. However, the literature on this area is still confusing, and more detailed studies are required. What is it about a confiding relationship that is protective? Can patients be helped to develop such ties when they are absent? Is there a circular relationship – in other words, does depression damage a confiding liaison? How do life events other than the cancer illness interplay in the aetiology of psychological disturbance? We look forward to good research studies from both Dr Ramirez and others to start to answer many of the questions she has raised in this deceptively straightforward account.

References

Cassileth, B. R., Lusk, E. J., Miller, D. S., *et al* (1985) Psychosocial correlate of survival in advanced malignant disease? *New England Journal of Medicine*, **312**, 1551–1555.

Dean, C. (1987) Psychiatric morbidity following mastectomy: preoperative predictors and types of illness. *Journal of Psychosomatic Research*, **31**, 385–392.

Devlen, J., Phillips, P. & Crowther, D. (1987) Psychological problems associated with the diagnosis and treatment of lymphomas. I. A retrospective study. II. A prospective study. *British Medical Journal*, **295**, 953–954, 955–957.

Fallowfield, L. J., Baum, M. & Maguire, G. P. (1986) Effects of breast conservation on psychological morbidity associated with diagnosis and treatment of early breast cancer. *British Medical Journal*, **293**, 1331–1334.

Greer, S., Morris, T. & Pettingale, K. W. (1979) Psychological response to breast cancer: effect on outcome. *Lancet*, *ii*, 785–787.

Hislop, T. G., Waxler, N. E., Coldman, A. J., *et al* (1987) The prognostic significance of psychosocial factors in women with breast cancer. *Journal of Chronic Diseases*, **40**, 729–735.

Holland, J. C., Korzun, A. H., Tross, S., *et al* (1986) Psychosocial factors and disease free survival (DFS) in stage II breast carcinoma. *Psychosocial Aspects of Cancer*, **5**, 237.

Jensen, M. R. (1987) Psychobiological factors predicting the course of breast cancer. *Journal of Personality*, **55**, 317–342.

Levy, S. M., Heberman, R. B., Maluish, A. N., *et al* (1985) Prognostic risk assessment in primary breast cancer by behavioural and immunological parameters. *Health Psychology*, **4**, 99–113.

Morris, T., Greer, S. H. & White, P. (1977) Psychological and social adjustment to mastectomy. *Cancer*, **40**, 2381–2387.

Pettingale, K. W., Morris, T., Greer, S., *et al* (1985) Mental attitudes to cancer: an additional prognostic factor. *Lancet*, *i*, 750.

Ramirez, A. J. (1989) Liaison psychiatry in a breast cancer unit. *Journal of the Royal Society of Medicine*, **82**, 15–17.

Renneker, R. & Cutler, M. (1952) Psychological problems of adjustment to cancer of the breast. *Journal of the American Medical Association*, **148**, 833–838.

Pettingale, K. W., Philalithis, A., Tee, D. E. H., *et al* (1981) The biological correlates of psychological response to breast cancer. *Journal of Psychosomatic Research*, **25**, 453–458.

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Case Conference

Self-Neglect and Frontal Lobe Dysfunction

MARTIN W. ORRELL, BARBARA J. SAHAKIAN and KLAUS BERGMANN

An elderly lady, of superior verbal intelligence and with no severe psychiatric condition, severely neglected herself, and required prolonged day patient care. Brain scans showed selective frontal atrophy, and both traditional and new computerised neuropsychological testing demonstrated severe frontal dysfunction.

Objectives

This is a report of a clinical case presentation from the Special Problems Conference held at the Institute of Psychiatry on 29 February, 1988. The conference, chaired by Professor Russell, was asked to examine any relationship between the patient's severe self-neglect and her frontal lobe dysfunction. Were the two entirely coincidental? Were either or both related to her drug and alcohol abuse? Was an underlying physical illness responsible? Was the self-neglect the result of stressful life experiences interacting with pain and some physical disability in someone with a long-standing personality disorder, or could specific frontal pathology adequately explain the deterioration in her level of functioning?

Presentation of case

The full history as presented below was obtained from the patient, her son, her social worker, and past medical records.

Mrs G, aged 80, was admitted as a day patient in August 1986 following a referral from her general practitioner and a subsequent consultant domiciliary visit, after she had come to the attention of the social services. In the previous three months she had had a number of falls, her hearing had become worse, and she started losing interest in life. She became aggressive towards her family and her home-help, and neglected her personal hygiene. She ate poorly, often instead giving money to her son and grandson, or spending it on Codis tablets (aspirin and codeine phosphate) and lager. She had been losing weight, was malnourished and incontinent, but refused to use the toilet. Her flat was squalid, with cigarette ends, rotting, uneaten meals, and excrement from her pekinese lying around. She seemed largely unaware of her state of self-neglect.

Family history

Her father, a bookmaker, died aged 85, after a stroke. He had abused alcohol and been in prison twice. Her mother died at the age of 67 from breast cancer; she was described as artistic, delicate, and highly strung. The patient was the youngest of seven siblings, three of whom were still alive, although she had no contact with them. Two sisters were reported to have had agoraphobia.

Personal history

Mrs G was born in 1908 and brought up in south London, but her childhood was marred as her mother was cold and aloof, and her father "used to shout a lot". At school she was academically average, but popular, and enjoyed sport and music; she left at the age of 14. She had had a number of jobs, but until her marriage in 1932, aged 24, she mainly helped her mother with the housekeeping. During World War II she worked as a postwoman, and then as an assistant to her husband, a dental technician. From 1950 she was a pianist in a public house. There were sexual difficulties in the marriage, and her husband tended to live his own life. He died in 1969 at the age of 61 of a myocardial infarction. Their only child was born by Caesarean section in 1939. The son said that his own marriage broke up as a result of interference by the patient, and he found it difficult to cope with her. She described her past personality as sociable, artistic, and idealistic. Her son described her as difficult, argumentative, and moody, and said she had antagonised friends and relatives.

Medical and psychiatric history

Aged about 70, Mrs G suffered a series of falls which resulted in arm and leg fractures, as well as a fractured right hip, for which she received a hip replacement. Since then she had had some difficulty walking and used a frame; she also suffered from arthritis.

At the age of 38 she received out-patient treatment for agoraphobia and marital problems, and began taking Drinamyl (dexamphetamine and amylobarbitone). She was seen on a number of occasions over the next two years, and attended a day hospital for a short time. In 1969, shortly after her husband's death, she requested Drinamyl, which she said she could no longer obtain from her general practitioner, from an emergency clinic.

She was an in-patient at the Maudsley in 1978 and again in 1979 because of severe alcohol abuse and self-neglect, in addition to personality disorder. She now smoked 20 cigarettes a day and drank three or four cans of lager, as well as taking Codis tablets when she could afford them. She lived in a large detached house with her son, grandson, and 18-year-old pekinese. The house was in danger of being repossessed because her son had persuaded her to make him part-owner and then taken out a mortgage upon which he had defaulted. She had no friends outside hospital. She frequently had arguments with the home-helps about what had been bought for her, which resulted in a number of them leaving. She repeatedly refused to pay for the meals-on-wheels service, which resulted in it being withdrawn, although she denied not having paid for them. The house remained in poor condition, with rotting woodwork, bare floor-boards, and damp carpets.

Mental state examination

Mrs G's mental state had changed little over the past 18 months. She was thin, and her clothes were sometimes dishevelled. She enjoyed conversation and maintained adequate rapport. Her current worries were over money, and the possible repossession of her house. She also complained of back pain and of her home-help not buying her pain killers. However, she was still able to be cheerful and she was not clinically depressed. Sometimes she was disinhibited, but she was not thought disordered, and suffered no abnormal beliefs or experiences. Her thought content was normal, and she had no obsessions or compulsions. Her general cognitive function was normal. She understood why she attended the day hospital, but did not fully appreciate her role in the continuing crises, her general self-neglect, or her social deterioration.

Physical examination

On admission she was cachectic, with rheumatoid deformities in both hands and mild heart failure. At the time of the case conference she was not in heart failure, but remained cachectic. No neurological abnormalities were elicited. Her weight had decreased from 44 to 41 kg.

Investigations

Comprehensive blood tests and ECG were normal. Occasional urinary tract infections responded to treatment with antibiotics. EEG showed non-specific mild diffuse dysfunction. X-rays revealed degenerative changes in the lumbar spine, and sequential chest X-rays showed a soft-tissue opacity in the left mid-zone centrally, which had slightly increased in size over the previous 18 months. The Chest Unit at King's College Hospital advised that while she was asymptomatic, further investigation was inappropriate, as it was likely to be a slow-growing squamous carcinoma, and any treatment might do more harm than good. A computerised tomography brain scan showed mild cerebellar atrophy, and marked but localised atrophy of the frontal lobes. Appearances were unchanged over 18 months.

Neuropsychological assessment

Two months following admission (October 1986), Mrs G was given a detailed neuropsychological assessment, including the short form of the Wechsler Adult Intelligence Scale (WAIS), the Kendrick Cognitive Tests for the Elderly, the Wisconsin Card Sorting Test (WCST), and the Word Fluency Test. Her pro-rated verbal IQ of 128 placed her in the superior range, and her pro-rated performance IQ of 94 was in the average range, the 34-point discrepancy being significantly abnormal. Her scores on both the Kendrick Object Learning Test (KOLT) and the Kendrick Digit Copying Test (KDCT) were within the non-dementing range, with age-scaled quotients of 95 and 93, respectively. She showed impairments on both traditional tests of frontal lobe function, the WCST and the Word Fluency Test, with performance on the former being similar to that of patients with frontal damage, and performance on the latter being closest to that of elderly depressed patients. On the WCST, she was able to obtain only one category, and she had a high ratio of perseverative errors to total errors on both the Nelson and Milner methods of scoring, performance typical of patients with frontal damage (Lezak, 1983). On the Word Fluency Test, she made one repetition within each category. In February 1988, she was given Thurstone's Word Fluency Test, and her performance was impaired, similar to that of patients with left frontal damage. She also made six repetitions.

In addition to the traditional neuropsychological tests, in February 1988, Dr Sahakian also gave Mrs G three tests of Planning and Spatial Working Memory (CANTAB) which utilise a microcomputer and a visual display unit (VDU) with a touch-sensitive screen (Morris *et al*, 1987, 1988). (a) The computerised Corsi Block Span Test, based on the block-tapping test of Corsi (Milner, 1971), is a test of spatial memory span. It was chosen as a simple index of the patient's ability to retain and execute a short sequence of spatial moves, an ability which is impaired in patients with right hippocampal lesions (Milner, 1971). (b) The Working Memory Test measures spatial working memory, and is related to the Olton Radial Arm Maze Test (Olton, 1982). A similar test is sensitive to lesions in the sulcus principalis area of pre-frontal cortex in non-human primates (Passingham, 1985). (c) The Computerised Tower of London Test, an adaptation of the human neuropsychological test developed by Shallice (1982), assesses planning deficits in patients with frontal lobe disorders. In the computerised version of this test, the patient is shown a display of coloured balls at the top of the VDU and is asked to think, plan, and then move the coloured balls in the display at the bottom of the screen until the display is identical to that at the top, within a specified number of moves.

While Mrs G's visuospatial span was not impaired, her ability to utilise and execute the low-level strategies required for efficient searching was impaired, as was her higher-level planning. Indeed, of the ten problems on the Tower of London Test, she was able to complete only three within the required number of moves. Furthermore, in the course of problem solving, she showed a substantial number of rule breaking and perseverative errors, behaviour indicative of frontal lobe dysfunction.

Interview

PROF. RUSSELL: Hello, have we met before?

MRS G: Yes we have, some time ago.

PROF. RUSSELL: You've got a hearing aid haven't you?

MRS G: Yes, we had some problems with it last time I spoke to you.

PROF. RUSSELL: I fixed it, didn't I?

MRS G: No, you didn't, I found out later there was a piece of paper stuck in it.

PROF. RUSSELL: I want to know how you're getting on.

MRS G: Bloody terrible: they're taking my house after 30 years – my stupid son, the house is going because he hasn't paid the debt.

PROF. RUSSELL: Has this anything to do with you being unable to look after the house?

MRS G: No, I keep myself clean, and these home-helps come in; no, that's got nothing to do with it doctor.

PROF. RUSSELL: I heard that you weren't well enough to look after it properly.

MRS G: I haven't any money, I've been feeling hungry. I haven't always got food to eat doctor.

PROF. RUSSELL: Yes, but you do drink?

MRS G: I've got a beautiful pekinese dog, he's 18 years old.

PROF. RUSSELL: I was asking you about drinking alcohol.

MRS G: Oh it's only lager – I used to drink whisky.

PROF. RUSSELL: Do you know what day it is today? [29 February].

MRS G: Yes, it's leap year – have you been leapt on?

PROF. RUSSELL: You sound very cheerful today.

MRS G: I might look cheerful but I feel terrible; my son wants his backside kicked.

Professor Russell examined Mrs G for cerebellar signs, but none were elicited, and since she had come to the conference in a wheelchair, she was asked to show how she was able to walk with a little assistance. He also asked her whether she minded if one of the other doctors asked her a question. She replied that she did not. Dr Post then attempted to elicit any lability of mood, since she seemed euphoric.

DR POST *(emeritus consultant psychiatrist)*: You say that you appear cheerful but deep down you are miserable. What was the worst moment in your life?

MRS G: Having my hip broken after I tripped over a hole in the pavement at the Borough.

DR POST: Are you sure that was the worst moment?

MRS G: Yes, how would you feel if you had broken your hip? Only the day before I was climbing an apple tree and now I can hardly walk!

During the course of the interview Mrs G appeared to enjoy being the centre of attention. As illustrated above, she was disinhibited at times, although her mood was not labile. Her memory and orientation were not abnormal, and she talked about the kind treatment she had received at this hospital.

Conference discussion

PROF. LISHMAN *(professor of neuropsychiatry)*: There are two possibilities regarding diagnosis: either there is no psychiatric diagnosis but what we are seeing is an elderly woman with learned helplessness, because her son has wrecked her final years of peace so that she has suffered a series of very traumatic life events; but the other, much more likely diagnosis is one of organic brain pathology, and unusual frontal atrophy which has resulted in a circumscribed neuropsychological deficit. This may, for example, be a case of very late onset Pick's disease, or related to her excessive alcohol consumption. On the other hand, it may in some way be related to the presumptive lung carcinoma. There does not seem to be a history of transient confusional episodes which may have supported the latter possibility.

DR CYBULSKA *(consultant psychiatrist with an interest in Diogenes syndrome)*: Clinically this patient has much in common with senile breakdown syndrome, as described by MacMillan, or the Diogenes syndrome, described by Clarke. These were the only two major studies of self-neglect in old age in the UK, and even in severe self-neglect around half of those studied had no psychiatric disorder and were generally of higher than average intelligence. It has been suggested that the syndrome may be a reaction late in life to stress, particularly to bereavement, in a certain type of personality.

Dr Cybulska asked Dr Sahakian whether she thought that the perseverative behaviour shown on the computerised test could be regarded as another form of the stereotyped behaviour seen in patients with these types of syndromes, such as stereotyped collecting or hoarding of objects. Dr Sahakian thought that it could.

DR POST: The Diogenes term is inappropriate in this case since the patient is not reclusive, and obviously enjoys company. It is difficult to know what the original psychiatric disorder was, since she has a long history of psychiatric disorders. The frontal changes may be long-standing and secondary to toxic damage by drugs or alcohol. With regard to Pick's disease this would be a very unusual course, and so I think that diagnosis is unlikely.

DR JANOTA *(senior lecturer in neuropathology)*: I can only speculate on the pathological abnormality causing the frontal atrophy. Is it possible that she did not react appropriately to the stink in her house because of anosmia, which may be a sign of a basal meningioma? It would be very unusual for the brain atrophy to have been caused by alcohol. A remote effect of a carcinoma is unlikely, but it is just possible that some form of carcinomatous encephalitis affecting the anterior temporal or the posterior frontal region may be responsible. There is a link with cerebellar atrophy, which is sometimes associated with a carcinoma.

PROF. LEVY *(professor of geriatric psychiatry)*: A group of clinicians and neuropathologists in Lund, Sweden, have suggested that in primary dementia there may be a subgroup of up to 15% with localised frontal pathology of neither Pick's disease nor Alzheimer's disease. The changes appear to be non-specific, and this patient appears to fit in with their view. [Gustafson, 1987; Englund & Brun, 1987]

DR BERGMANN *(consultant in charge of the case)*: It is difficult to be specific about the nature of the chest lesion, although it may have given rise to non-metastatic central nervous system complications of carcinoma.

DR POST: Even so, there is no way we have of demonstrating carcinomatosis in this lady.

PROF. LISHMAN: I am not aware that severe self-neglect with a selective frontal problem has been described before.

In the concluding remarks, Dr Bergmann suggested that in many cases of senile self-neglect, organic dementia or a functional psychosis is not evident. Where they are evident, although a necessary feature, they do not seem sufficient to explain the manifestations of extreme self-neglect. Where personality disorder is the only manifestation that can be detected, it is even less of a sufficient explanation for the syndrome.

It is suggested that for some cases at least, frontal lobe deficits may be the missing factor in accounting for this mysterious condition. Regarding further investigations, Dr Janota suggested that a magnetic resonance scan would have been useful, to try to delineate more clearly the frontal pathology.

Discussion

The first major study on gross self-neglect in the elderly (Macmillan & Shaw, 1966) found that a large proportion of the patients were not suffering from psychosis, but were described as having certain personality characteristics in common. In particular, a hostile attitude and resistance to help were noted, and the individuals were often described as stubborn, obstinate, aloof, suspicious, and aggressive. A similar pattern was also described by Clarke *et al* (1975), who noted that the patients seemed to show lack of shame about their state of physical hygiene, and sometimes hoarded rubbish. In addition, roughly half of these patients showed no evidence of psychiatric disorder and had higher than average intelligence, many having led successful lives. It was suggested that this pattern could be a reaction late in life to stress in a certain type of personality, and it was labelled 'Diogenes syndrome', after the ascetic Greek philosopher who lived as a vagabond beggar, and supposedly slept in a barrel. However, the term 'Diogenes' and even the validity of describing it as a separate syndrome have been questioned by Post (1982), who argued that it is merely the end-stage of a personality disorder, the patient being best described as a 'senile recluse'. Cybulska & Rucinski (1986) point out that it is probably aetiologically heterogeneous. However, perhaps the most important point is that a large proportion of the cases appear to be suffering either from no psychiatric disorder, or from a disorder which is not sufficiently severe to explain their extreme social deterioration.

Although the case conference discussed this woman's self-neglect in relation to a personality disorder, and the frontal atrophy in relation to the neuropsychological deficits, as well as the possible underlying pathology of this, it did not clearly address the question of a relationship between the frontal dysfunction and her self-neglect. However, there are certain aspects of the frontal lobe syndrome (Lishman, 1987) which typify this particular patient, and are also surprisingly similar to many of the personality characteristics described in gross self-neglect. When interviewed, the patient was boisterous and overfamiliar, showing a disinhibition and lack of tact. Her mood was irritable and somewhat incongruous when asked about distressing events. From her history it seemed clear that her judgement was poor, and she was unable to plan effectively or predict the consequences of her actions. In addition, she suffered from lack of initiative, and seemed unable to complete simple tasks associated with her self-care. Frontal damage can also result in hostility and aggression, and paranoid ideas.

Amphetamine addiction may produce perseverative and stereotyped actions and thoughts, as well as paranoid ideation (Connell, 1958; Rylander, 1971), and the similarity to frontal lobe dysfunction has been noted (Ridley & Baker, 1982; Robbins *et al*, 1989). Chronic alcohol abuse can impair performance on problem-solving tasks, including the Wisconsin Card Sort Test (Butters, 1985). However, it is unlikely that her history of substance abuse would account for such marked frontal dysfunction, especially as there were no major physical sequelae suggestive of severe alcoholism.

'Dementia of frontal lobe type' has been described by Neary *et al* (1988). It is characterised by social misconduct, personality change, and disinhibition in general, but attention remains intact, and memory impairment is variable. Several patients exhibited marked self-neglect.

Neuropsychological testing revealed frontal deficits, as did single-photon emission tomography studies. In Neary *et al*'s series of 138 dementia cases, almost 25% were classified as dementia of frontal lobe type. Although there were many similarities between our patient and their patients, verbal IQ was spared, and Mrs G was not diagnosed as having dementia. It will however be of great interest to determine whether in follow-up her cognitive function declines.

Although only Macmillan & Shaw (1966) made an extensive inquiry into the patient's previous personality by interviewing relatives, neighbours, and friends, as well as obtaining written information from other sources, it is not clear whether this was, in the majority of cases, a good description, since the individual may have been in a gradual state of deterioration for several years. Lishman (1987) points out that the previous personality may be important in determining the particular presentation of patients suffering from frontal lobe damage. Two other patients who have been previously admitted to the Felix Post Unit suffering from severe self-neglect also showed signs of frontal dysfunction on neuropsychological testing, and one of these, in addition, had evidence on computerised tomography of specific frontal damage. It is suggested that in some cases of severe self-neglect in elderly patients without psychiatric disorder of a sufficient severity to explain the gross deterioration, underlying frontal lobe dysfunction may play an important part in their decline.

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References

Butters, N. (1985) Alcoholic Korsakoff's syndrome: some unresolved issues concerning aetiology, neuropathology and cognitive deficits. *Journal of Clinical and Experimental Neuropsychiatry*, 7, 181–210.

Clarke, A. N. G., Mankikar, G. D. & Gray, I. (1975) Diogenes syndrome: a clinical study of gross self-neglect in old age. *Lancet*, *i*, 366–368.

Connell, P. H. (1958) *Amphetamine Psychosis*. Maudsley Monographs No. 5. London: Chapman and Hall.

Cybulska, E. & Rucinski, J. (1986) Gross self-neglect in old age. *British Journal of Hospital Medicine*, July, 21–25.

Englund, E. & Brun, A. (1987) Frontal lobe degeneration of non-Alzheimer type. IV. White matter changes. *Archives of Gerontology and Geriatrics*, 6, 235–244.

Gustafson, L. (1987) Frontal lobe degeneration of non-Alzheimer type. II. Clinical picture and differential diagnosis. *Archives of Gerontology and Geriatrics*, 6, 209–224.

Lezak, M. D. (1983) *Neuropsychological Assessment*. Oxford: Oxford University Press.

Lishman, W. A. (1987) *Organic Psychiatry*. Oxford: Blackwell Scientific Publications.

Macmillan, D. & Shaw, P. (1966) Senile breakdown in standards of personal and environmental cleanliness. *British Medical Journal*, *ii*, 1032–1037.

Milner, B. (1971) Interhemispheric differences in the localisation of psychological processes in man. *British Medical Bulletin*, 27, 272–277.

Morris, R. G., Evenden, J. L., Sahakian, B. J., *et al* (1987) Computer aided assessment of dementia: comparative studies of neuropsychological deficits in Alzheimer type dementia and Parkinson's disease. In *Cognitive Neurochemistry* (eds S. M. Stahl, S. D. Iversen & E. C. Goodman). Oxford: Oxford University Press.

——, Downes, J. J., Sahakian, B. J., *et al* (1988) Planning and spatial working memory in Parkinson's disease. *Journal of Neurology, Neurosurgery and Psychiatry*, 51, 757–766.

Neary, D., Snowden, J. S., Northern, B., *et al* (1988) Dementia of frontal lobe type. *Journal of Neurology, Neurosurgery and Psychiatry*, 51, 353–361.

Olton, D. S. (1982) Spatially organised behaviours of animals: behavioural and neurological studies. In *Spatial Abilities* (ed. M. Potegal). London: Pergamon.

Passingham, R. E. (1985) Memory of monkeys (*Macaca Mulata*) with lesions in the prefrontal cortex. *Behavioural Neurosciences*, 99, 3–21.

Post, F. (1982) Functional disorders I. Description, incidence and recognition. In *The Psychiatry of Late Life* (ed. R. Levy & F. Post). London: Blackwell Scientific Publications.

Ridley, R. M. & Baker, H. F. (1982) Stereotypy in monkeys and humans. *Psychological Medicine*, 12, 61–72.

Robbins, T. W., Mittleman, G., O'Brien, J., *et al* (1989) The neuropsychological significance of stereotypy induced by stimulant drugs. In *Neurobiology of Stereotyped Behaviour* (eds S. Cooper & C. Dourish). Oxford: Oxford University Press. (In press).

Rylander, G. (1971) Stereotype behaviour in man following amphetamine abuse. In *The Correlation of Adverse Effects in Man with Observation in Animals* (ed. S. B. de C. Baker). Amsterdam: Excerpta Medica.

Shallice, T. (1982) Specific impairments of planning. *Philosophical Transactions of the Royal Society of London*, B298, 199–209.

Whitehead, A. (1985) Diogenes syndrome (letter). *Lancet*, *i*, 627–628.

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Minaprine: An Anticholinergic-Free Antidepressant?
Results of a Controlled Trial of Mianserin

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Minaprine is an amino-phenylpyridazine antidepressant reported to be relatively free of anticholinergic effects, cardiotoxicity, drowsiness, and weight gain. Minaprine (100 mg t.d.s. and 100 mg b.d.) was compared with mianserin (20 mg t.d.s.) in 117 depressed patients, and all three regimes produced significant reductions in scores on the HRSD at the end of six weeks' treatment. There were no anticholinergic effects, but there was a significantly greater incidence of drowsiness with mianserin than with minaprine.

The introduction of a new antidepressant is justified if it has advantages over those already in use, but so far no new drug has proved to be more efficacious than its forerunners (Paykel, 1985). However, new compounds may bestow 'fringe benefits' in relation to side-effects and, in particular, anticholinergic effects, cardiotoxicity, drowsiness, and weight gain may cause problems with established drugs.

Minaprine is an amino-phenylpyridazine compound which facilitates serotonergic, dopaminergic, and cholinergic transmission. The chemical configuration is shown in Fig. 1. The compound has been shown to exert antidepressant effects in experimental studies (Biziere *et al*, 1982) and in clinical trials against placebo (Jouvent *et al*, 1984), imipramine and maprotiline (Radmayr *et al*, 1984) and nomifensine (Mikus *et al*, 1984). These studies have demonstrated freedom from all the adverse effects mentioned above. Mianserin is relatively free from anticholinergic effects and cardiotoxicity, but often causes drowsiness and weight gain, and so was chosen as the comparative drug for this study.

The trial

European studies have indicated the effective dose range to be 200–300 mg daily, such side-effects as occurred being dose-related (Biziere *et al*, 1985). Since adverse events may affect patient compliance in general practice (Wheatley, 1987), a parallel group, randomly assigned double-blind trial was undertaken to compare minaprine (100 mg t.d.s. and 100 mg b.d.) with mianserin (20 mg t.d.s.) (10 mg t.d.s. for patients aged 65 years and over). The drugs were supplied in matching capsules, one week's supply at a time, and capsules were counted at the end of each assessment period, to check patient compliance. The trial was undertaken by 13 general practitioner members of the group, who treated 117 depressed patients for six weeks; DSM–III criteria (American Psychiatric Association, 1980) were used, with a minimum score on the Hamilton Rating Scale for Depression (HRSD; Hamilton, 1967) of 19 or more. Those taking part had previously attended training sessions to validate inter-rater reliability in completing the HRSD.

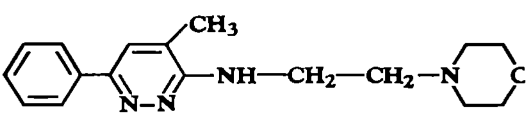

FIG. 1 *Formula of minaprine: 3 – (2N morpholino) ethylamino, 4–methyl, 6–phenyl pyridazine, dihydrochloride.*

Patients were excluded if they were suffering from schizophrenia, chronic brain syndrome, senile dementia, epilepsy, cardiac, renal or hepatic failure, or peptic ulcer, as were women who might be pregnant or breast feeding. Furthermore, patients were excluded if they were being treated with lithium, had an abnormal EEG or ECG, or were suicidal. Written informed consent was obtained from all patients before the start of the trial.

Predictably, females outnumbered males; the sex ratios for the three groups were minaprine (t.d.s.) 3 : 1, minaprine (b.d.) 5.5 : 1, and mianserin 3.2 : 1. In the three groups respectively, the mean ages were 57.0, 51.7 and 55.9 years, the mean durations of the present depressive episode 19.4, 10.1, and 18.8 weeks, and incidence of previous attacks 45%, 59% and 55%.

Results

The full six-week trial was completed by 34 patients in the minaprine (t.d.s.) group, 28 in the minaprine (b.d.) group, and 32 in the mianserin group. The 'last visit carried forward' (LVCF) method was used for another eight patients who completed at least three weeks (two in the minaprine (t.d.s.) group, four in the minaprine (b.d.) group, and two in the mianserin group), and these were included in the analysis. Otherwise, there were five drop-outs in the minaprine (t.d.s.) group, nine in the minaprine (b.d.) group, and four in the mianserin group, leaving 99 patients for analysis. The paired *t*-test was used to test for pre–post differences, and the *t*-test for

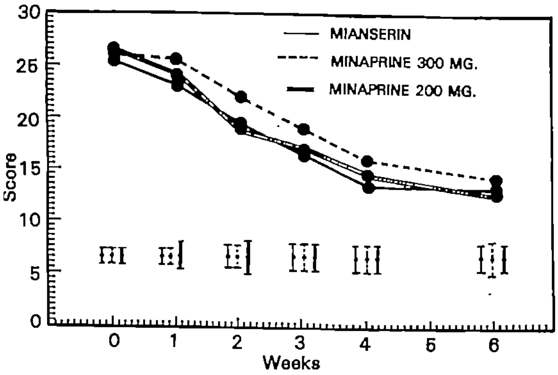

FIG. 2. *Reduction in mean HRSD scores during the trial* (——, mianserin; – – –, minaprine (100 mg t.d.s.); ═, minaprine (100 mg b.d.)). Error bars indicate s.e.m.s.

between-group differences. The results are shown graphically in Fig. 2.

There was a highly significant reduction in mean HRSD scores at all periods ($P<0.01$) except from week 0 to 1 in the minaprine (t.d.s.) group only.

However, mean scores do not necessarily represent the true picture of antidepressant drug effects, and different categories of response should also be considered. According to Hamilton (1987, personal communication) a final score of 6 or less on the HRSD can be considered as 'symptom-free', while end-points between 7 and 18 (minimum score for entry was 19) would represent 'improvement', and a final score of 19 or more, 'no change or worse'. Using these criteria, at the end of the trial the proportions of 'symptom-free' were: minaprine (t.d.s.) 4 (11%), minaprine (b.d.) 8 (27%), and mianserin (10) (29%); 'improved': 22 (63%), 17 (57%), and 17 (50%) respectively; and 'failures' 9 (26%), 5 (17%), and 7 (21%) respectively.

Side-effects

The only side-effect of any importance was drowsiness or tiredness which, allowing for baseline incidence, occurred in no patients on minaprine (t.d.s.), 4 (10%) on minaprine (b.d.), and 6 (16%) on mianserin ($P<0.05$, χ^2). The only anticholinergic effects recorded were two cases of dry mouth on minaprine (b.d.), and one on mianserin. Otherwise, there were only two cases of 'irritability' in the minaprine (t.d.s.) group, with no other side-effects of any importance.

Discussion

Relief of depression was virtually identical between both doses of minaprine and the control drug mianserin, with the usual delayed onset of therapeutic effect and proportion of poor responders in all three groups. Although the proportion of patients rendered 'symptom-free' was lower in the minaprine (t.d.s.) group than in either of the other two groups, the differences are not statistically significant (χ^2). Although the occurrence of anticholinergic effects was negligible with either minaprine or mianserin, there was a significantly increased incidence of drowsiness with the control drug. Furthermore, a disadvantage of mianserin is the necessity to undertake a monthly haematological screening which, in the present climate of public opinion concerning psychotropic drugs, may have an adverse effect on patient compliance. Although we did not measure weight during the trial, weight gain can be a troublesome side-effect with most antidepressant drugs, and can sometimes nullify the improvement in depressive symptoms, particularly in female patients, who can experience a return of depression as their girth increases (personal observations).

This is a relatively small sample, but if the freedom from unwanted effects with minaprine is confirmed in further trials, then it should prove to be a useful addition to the antidepressant drug spectrum.

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References

AMERICAN PSYCHIATRIC ASSOCIATION (1980) *Diagnostic and Statistical Manual of Mental Disorder* (3rd edn) (DSM-III). Washington, DC: APA.

BIZIERE, K., KAN, J. P., SOUILHAC, J., *et al* (1982) Pharmacological evaluation of minaprine dihydrochloride, a new psychotropic drug. *Arzneimittelforschung/Drug Research*, **32**, 824–831.

——, BLANC, F., CAUTREELS, W., *et al* (1985) *Minaprine: Investigator's Brochure*, pp. 132–198. Wythenshawe, Manchester: Sanofi UK.

HAMILTON, M. (1967) Development of a rating scale for primary depressive illness. *British Journal of Social and Clinical Psychology*, **6**, 278–296.

JOUVENT, R., LANCRENON, S., PATAY, M., *et al* (1984) A controlled study of minaprine versus placebo in inhibited depressed outpatients. *Recent Advances in Psychiatric Treatment*, pp 33–40. Montpelier: Sanofi Recherche.

MIKUS, P., BIZIERE, K. & BENTEL, U. (1984) Double-blind study of minaprine versus nomifensine in patients with a masked depression. *Recent Advances in Psychiatric Treatment*, pp 41–54. Montpelier: Sanofi Recherche.

PAYKEL, E. S. (1985) How effective are antidepressants? In *Psychopharmacology: Recent Advances and Future Prospects* (ed. S. D. Iversen), pp. 3–13. Oxford: Oxford University Press.

RADMAYR, E., BIZIERE, K. & BENTEL, U. (1984) Comparative effects of mina prine and maprotiline in depressed inhibited patients. A double-blind study. *Recent Advances in Psychiatric Treatment*, pp 55–61. Montpelier: Sanofi Recherche.

WHEATLEY, D. (1987) Psychopharmacology in the real world. *Human Psychopharmacology*, **2**, 195–196.

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Trichotillomania and Incest

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Trichotillomania is reported in a 33-year-old female victim of incest, with a possible causal connection.

The French dermatologist Hallopeau (1889) first coined the term 'trichotillomania' to describe compulsive hair pulling, mainly from the scalp area, but which can also involve other areas, such as eyebrows, eyelashes, pubic hair, and beard. It usually presents in adolescence, although occasionally children may also be affected. Female hair pullers are predominent. It appears to be related to stress, varying in duration from weeks to years, and in isolated cases the hair, which may be pulled singly or in tufts, is collected, and may even be swallowed, with subsequent intestinal complications.

Tricotillomania has been reported in the context of many psychopathological processes, and has been described as an obsessive–compulsive disorder (Philippopoulos, 1961), a neurotic trait (Seitz, 1950; Sperling, 1954; Gerard, 1953), a tension-reducing habit (Gelder *et al*, 1983), fetishism (Buxbaum, 1960), masochistic behaviour (Oguchi & Miura, 1977), denial of femininity, masturbatory equivalent, and castration equivalent. It has been reported in a variety of psychiatric disorders, notably schizophrenia, borderline state, and depression (Greenberg & Sarner, 1965). Bartsch (1956) suggested a possible organic aetiology resulting from motor discharges originating in subcortical regions. It is also known to occur in the mentally retarded (Gelder *et al*, 1984).

The prognosis is always guarded, as reports suggest (Mannino & Delgado, 1969) that no one treatment modality has been successful. Many approaches have been attempted, for example, treatment with chlorpromazine (Childers, 1958), psychotherapy (Stockmann, 1962), psychoanalysis (Monroe & Abse, 1963), and behavioural methods, among others (Deluca & Holborne, 1984). Here we present what we believe to be the first report of a case of trichotillomania in an incest victim.

Case report

A 33-year-old woman presented for the first time to our services in May 1983 for assessment of compulsive hair pulling from her scalp. She was noted to have significant depressive features, mainly reactive in nature, with vague suicidal ruminations. She commenced amitriptyline (75 mg *nocte*), but defaulted from follow-up almost immediately. She was referred two years later, three weeks after the birth of her first child, a son by Caesarean section, with a post-partum depressive state, and she responded well to small doses of amitriptyline.

She had been continuously hair pulling since the age of 15 years. It had a marked compulsive quality to it. She described self-punitive impulses in association with the trichotillomania, and rationalised these on the basis that if she failed to continue hair pulling there might be ominous consequences for those around her. In her own words: "If I don't do it something terrible will happen to everybody, but not to me. That will be my punishment – left alone."

She was born fourth in a family of nine children. Her three older siblings, one brother and two sisters, were aged five years, four years and three years, respectively, at the time of her birth, which was by Caesarean section. Her mother, aged 27 years at that time, suffered perinatal brain damage. This rendered her unable to look after the child, and the patient was placed in institutional care until the age of 15 years. It is noteworthy that the other siblings and subsequent siblings, four girls and one boy born 2, 4, 11, 12, and 16 years later, were cared for at home.

Her father was aged 31 years at the time of her birth, a small farmer with little income. At that time he was already a well-established alcoholic, and despite his wife's ill-health continued to drink, making minimal efforts to maintain cohesion within the family. On further enquiries we discovered that our patient had been cared for by her grandmother for the first year of her life, but when she was seen to be developing rickets, she was placed in care, where she received neither letters nor gifts from her family, and was visited on only two occasions. She recalls her stay in care as being a happy one, with good adjustment and no obvious neurotic traits. This placement was unusual, in that she was the only child in the institution, was cared for by a religious order, and her only contacts were with lay and religious nursing staff and geriatric patients. She recalled a visit from her father when she was aged 15 years, and his insistence on taking her home "because he knew I was 15". Her father told her that he wanted to take her on a fortnight's holiday; according to our patient he raped her in a field, and refused to allow her to return to the institution. She received no further schooling, and was required almost exclusively to cater for the upkeep and management of the home and family. Her father continued to abuse her sexually over the ensuing seven years. Her older brother also indulged in regular sexual abuse shortly after her return home. It seems despite the fact that she had five sisters, she was the only victim of incest. She felt the reason that she was singled out was that she was never viewed as a member of the nuclear family, because of her long absence from home.

At the age of 22 years she became pregnant by her father, and following his attempts using traditional potions to induce abortion, she suffered a miscarriage. From this point onwards she rejected any further advances from her father and her brother. However, she stayed in the house, continuing to look after the family. Her father developed possessive, jealous feelings towards her, and refused to allow her to socialise or have any boyfriends. She tolerated this until she left the household at the age of 31 years. At this stage her trichotillomania was established for 16 years. In the year before she left home she was admitted on three occasions to a general hospital following overdoses. She said she intended to kill herself, as her role within the family was now becoming redundant – her younger brothers and sisters were becoming independent. She was seen by social workers during her admissions and arrangements were made for her to live in a flat of her own. She was very content with this arrangement and her new-found freedom, although she remained unemployed. She became pregnant by her first boyfriend, who left her when she told him. It was following the birth of this baby that she presented for the second time to our services.

As previously noted, her depression responded to amitriptyline, but her trichotillomania persisted. We initiated a treatment strategy of psychotherapy, with competing response training. She had had a short, brunette, male-type hairstyle at all stages of contact up to this point, and at the start of therapy she had multiple bald patches, averaging three inches in diameter, evenly distributed over her scalp. The initial objective was to re-enforce the positive aspects of her self-image and self-esteem. She was encouraged to pay particular heed to her grooming and make-up. She found this to have a positive effect on her sense of well-being, and after one month she spontaneously purchased a mid-length blonde wig, which enhanced her appearance dramatically. In the initial stages she had appeared motivated in using competitive response techniques, and her hair-pulling decreased considerably. She attended for regular psychotherapy, but it became clear after a number of weeks that she lacked consistent motivation, and she began to default before finally being lost to follow-up after a further two months.

Discussion

Hair has been traditionally viewed as a symbol of beauty and strength, and has played a major role in the myths and customs of many cultures (Barahal, 1940; Leach, 1958). Hair pulling by women can be viewed as displaced aggression, and an attempt to deprive themselves of their femininity (Oguchi & Miura, 1977). Several authors refer to sexual conflicts as being the basic psychopathological mechanism of trichotillomania; Berg (1936, 1951) suggested it to be a manifestation of an underlying conflict between sexual impulses at the genital level and the repressing forces of the superego or the ego; Barahal (1940) hypothesised that hair is a phallic symbol and disorders relating to it could thus be interpreted as indicative of poor sexual adjustment. Monroe & Abse (1963) again stressed sexual conflict as being an aetiologial feature of trichotillomania, and viewed it as a manifestation of self-castration or masturbatory impulses. Sperling (1954) suggested that in certain cases it symbolised unconscious bisexual conflicts; Zaidens (1951) viewed hair pulling in the scalp region as being more serious, and distinct from that in other areas; it represented in his case studies an attempt on the part of the patient to escape from intolerable sexual situations presented by marriage. This distinction was also made by Ilan & Alexander (1965), who took the view that trichotilloma of the scalp indicated pre-genital disturbances, involving deep regression. Irwin (1953) felt that hair pulling could be interpreted as an aggressive response to coping with grief and rage.

In our patient there would appear to be a relationship between her hair pulling and incest. Faced with the loss of her fantasised and idealised father figure and the reality of the return of a sexually aggressive father, with subsequent grief and rage, she introjected her aggression, and hence developed depressive ideation with parasuicidal behaviour. Her hair pulling could be viewed as a privatised magico-protective rite, or a maladaptive, masochistic attempt to deal with the conflict by denial of her femininity. Alternatively it could be interpreted as symbolising castratory impulses. Zaidens' (1951) view of trichotillomania of the scalp would account for this patient's attempts to escape from incest.

With the increasing number of reported cases of child sexual abuse, it is likely that more unusual presentations will emerge, and more vigilance is required. Sexual conflicts must always be considered when assessing trichotillomania.

References

Barahal, H. S. (1940) The psychopathology of hair plucking. *Psychoanalytic Review*, 27, 291–310.

Bartsch, E. (1956) Contribution towards the aetiology of trichotillomania in infancy. *Psychiatry, Neurology and Medical Psychology*, 8, 173–182.

Berg, C. (1936) The unconscious significance of hair. *International Journal of Psychoanalysis*, 17, 73–88.

—— (1951) *The Unconscious Significance of Hair*. London: George Allen & Unwin.

Buxbaum, E. (1960) Hair pulling and fetishism. *Psychoanalytic Study of the Child*, 15, 243–260.

Childers, R. T., Jr (1958) Report of two cases of trichotillomania of long standing duration and their response to chlorpromazine. *Journal of Clinical and Experimental Psychopathology*, 19, 141–144.

DELUCA, R. V. & HOLBORN, S. W. (1984) A comparison of relaxation training and competing response training to eliminate hair pulling and nail biting. *Journal of Behaviour Therapy and Experimental Psychiatry*, **15**, 67–70.
GELDER, M., GATH, D. & MAYOU, R. (1983) *Oxford Textbook of Psychiatry*. Oxford: Oxford University Press.
GERARD, M. W. (1953) Emotional disorders of childhood. In *Dynamic Psychiatry* (eds F. Alexander & H. Ross), pp. 165–211. Chicago: University of Chicago Press.
GREENBERG, H. R. & SARNER, C. A. (1965) Trichotillomania, symptom and syndrome. *Archives of General Psychiatry*, **12**, 482–489.
HALLOPEAU, X. (1889) Alopecia par grottage (trichomania ou trichotillomania). *Annals of Dermatology and Syphilis*, **10**, 440.
ILAN, E. & ALEXANDER, E. (1965) Eyelash and eyebrow pulling (trichotillomania): treatment of two adolescent girls. *Israel Annals of Psychiatry and Related Disciplines*, **3**, 267–281.
IRWIN, D. (1953) Alopecia. In *Emotional Factors in Skin Disease* (eds B. G. Russel & E. D. Wittkower), p. 179. New York: Paul Hoeber.
LEACH, E. R. (1958) Magical hair. *Journal of the Royal Anthropological Institute*, **88**, 147–164.
MANNINO, F. V. & DELGADO, R. A. (1969) Trichotillomania in children. A review. *American Journal of Psychiatry*, **126**, 505–511.
MONROE, J. T. JR & ABSE, D. W. (1963) The psychopathology of trichotillomania and trichophagy. *Psychiatry*, **26**, 95–103.
OGUCHI, T. & MIURA, S. (1977) Trichotillomania: its psychopathological aspect. *Comprehensive Psychiatry*, **18**, 177–182.
PHILIPPOPOULOS, G. S. (1961) A case of trichotillomania (hair pulling). *Acta Psychotherapeutica (Basel)*, **9**, 304–312.
SEITZ, P. F. (1950) Psychocutaneous conditioning during the first two weeks of life. *Psychosomatic Medicine*, **12**, 187–188.
SPERLING, M. (1954) The use of hair as a bisexual symbol. *Psychoanalytic Review*, **41**, 363–365.
STOCKMANN, F. (1962) Trichotillomania – a study in child psychiatry. *Praxis Kinderpsychology*, **11**, 281–290.
ZAIDENS, S. (1951) Self-inflicted dermatoses and their psychodynamics. *Journal of Nervous and Mental Disorders*, **113**, 400–402.

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Transient Recurrence of Auditory Hallucinations During Acute Dystonia

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Three schizophrenic patients who had transient recurrence of auditory hallucinations during acute dystonia precipitated by neuroleptic medication are reported. If it is accepted that psychotic symptoms result from dopaminergic overactivity, such phenomena suggest that acute dystonia might also have been caused by increased dopaminergic neurotransmission in these cases.

Acute dystonia occurs in 2–10% of patients receiving neuroleptic drugs (Swett, 1975). Its five commonest manifestations are oculogyric crisis, torticollis, contraction of the tongue, trismus, and opisthotonus (Mackay, 1982). Such drug-induced dystonia is seen more frequently in young males; it is rapidly relieved by anticholinergic medication (Roos & Buruma, 1984). However, the mechanism of drug-induced dystonia is still not well understood (Fahn & Marsden, 1987). There are two opposing hypotheses. One proposes that it is due to post-synaptic dopaminergic blockade by neuroleptics, resulting in imbalance between dopaminergic and cholinergic neurotransmission, similar to what happens in drug-induced Parkinsonism (Borison *et al*, 1982; Loudon, 1983; Hollister, 1983). The second hypothesis suggests that it results from initial pre-synaptic inhibitory dopaminergic receptor blockade by neuroleptics, leading to increased dopaminergic transmission (Silverstone & Turner, 1982; Hirsch, 1982; Grohmann *et al*, 1983; Roos & Bruyn, 1986). In the first hypothesis, anticholinergics are thought to act by restoring the balance between dopaminergic and cholinergic neurotransmission. In the second hypothesis, it is difficult to explain the mechanism of action of anticholinergics. In fact, besides anticholinergics, diphenhydramine (Smith & Miller, 1961), diazepam (Korczyn & Goldberg, 1972), or methylphenidate (Fann, 1966), given parenterally, can all promptly relieve acute dystonia, and Grohmann *et al* (1983) concluded that more than cholinergic effects were probably involved.

This paper reports three schizophrenic patients who had transient recurrence of auditory hallucinations during acute dystonia. If psychotic symptoms are accepted as being mediated through dopaminergic overactivity (Randrup & Munkvad, 1972), such phenomena suggest that acute dystonia is caused by increased dopaminergic neurotransmission.

Case reports

Case 1

Mr W is a 29-year-old, single, unemployed man, whose mother and older sister are known schizophrenics. Ten years ago, while working as an office messenger, the patient had insidious onset of social withdrawal, with frequent giggling. He heard voices of children commenting on his behaviour, and believed that his thoughts were transmitted to everyone around. He was diagnosed as having schizophrenia. His psychotic symptoms gradually remitted with trifluoperazine (20 mg per day) and benzhexol (8 mg per day), yet because of his poor drug compliance, his auditory hallucinations and delusions of thought broadcast soon recurred, and he has been admitted to a general hospital psychiatric ward four times during the past six years.

Two years ago, the patient was admitted into our psychiatric day hospital for rehabilitation, and was put on haloperidol decanoate (100 mg) together with benztropine (2 mg i.m.) once every four weeks. He no longer had delusions or hallucinations, except during three days after depot injections, when he always developed oculogyric crises, accompanied by auditory hallucinations. Yet when his oculogyric crises were treated with additional benztropine (2 mg i.m.), the hallucinations gradually disappeared. The patient was admitted to a psychiatric ward, the depot injections were stopped, and he was given thioridazine (250 mg per day) and benzhexol (8 mg per day orally); his oculogyric crises and hallucinations then ceased. One month later, he was discharged to a day hospital. Follow-up for seven months (up to the time of writing) revealed no further problems.

Case 2

Mr T is a 17-year-old, single, unemployed man, who emigrated from China to Hong Kong with his mother six years ago. The patient could not cope with the school work in Hong Kong. Two years ago, he believed that his classmates and teachers were all ghosts trying to harm him, and heard voices of classmates discussing him. The patient was diagnosed with schizophrenia. His psychotic symptoms subsided gradually with trifluoperazine (20 mg per day) and benzhexol (4 mg per day), yet after discharge, the patient idled at home and refused to take the drugs. His paranoid delusions and third-person auditory hallucinations gradually recurred. He was readmitted to our psychiatric ward a year ago, when haloperidol decanoate (50 mg) together with benztropine (2 mg i.m. once every 4 weeks) were administered. The delusions and hallucinations disappeared, except during the four days after depot injections, when he always developed oculogyric crises and torticollis, accompanied by auditory hallucinations, which subsided with additional benztropine (2 mg i.m.). After three such episodes, the patient refused to continue depot injections. Thioridazine (200 mg per day) and benzhexol (4 mg per day orally) were prescribed, and the patient had no more acute dystonia or hallucinations. Unfortunately, six months later, the patient stole female underwear from his neighbours. When his mother blamed him for this, he wounded her left arm with a chopper, and was admitted to mental hospital under a hospital order.

Case 3

Mr L is a 20-year-old, single, office assistant. Two years ago, while preparing for school certificate examination, the patient became very anxious, and could sleep only from about 3 a.m. to 7 a.m. He believed that the television company was watching him with electronic eyes, and he heard voices from the street gossiping about him. The patient was diagnosed with schizophrenia. His psychotic symptoms subsided gradually with trifluoperazine (10 mg) and benzhexol (4 mg b.d.). After two months of in-patient treatment, he was transferred to our psychiatric day hospital for rehabilitation, where the patient soon complained that two hours after taking the medication, his eyeballs would often roll up. Then he would hear voices from the street gossiping about him. When this happened, the patient would either take additional benzhexol (12 mg) himself, or go to the accident and emergency department to ask for an intramuscular injection of benztropine (2 mg). Because of the worry that the patient would become dependent on anticholinergics, his medication was changed to thioridazine (250 mg per day) and benzhexol (8 mg per day). The patient then had no more oculogyric crises or hallucinations. He has found a job as an office assistant and has been followed up at our clinic for six months without further problems.

Discussion

These three patients had been asymptomatic for more than four weeks when, on readministration of haloperidol decanoate or trifluoperazine, they developed acute dystonia with transient recurrence of auditory hallucinations. Both phenomena subsided promptly with anticholinergic medication or after changing to thioridazine, a low-potency neuroleptic. The repeated association of these two phenomena may be explained in three ways: (a) transient recurrence of auditory hallucinations caused acute dystonia; (b) acute dystonia caused transient recurrence of auditory hallucinations; or (c) a third factor caused both acute dystonia and transient recurrence of auditory hallucinations.

Transient recurrence of auditory hallucinations as a cause of acute dystonia can be easily dismissed, because the three patients had had auditory hallucinations before they developed acute dystonia after administration of neuroleptics. Moreover, auditory hallucinations have not been reported to be a cause of acute dystonia.

The second possibility is that acute dystonia caused the patients to become very anxious, resulting in transient recurrence of auditory hallucinations. In fact, anxiety as a cause of auditory hallucinations is suggested by studies on skin conductance (Cooklin *et al*, 1983), and self-report of mood disturbance (Slade, 1972). However, as most anxious people do not develop auditory hallucinations, anxiety is not a sufficient cause. Moreover, there would have to be some mediating biochemical processes. After an extensive review of many biochemical hypotheses, Walker & Cavenar (1983) concluded that the neurochemical explanation of hallucinations remained unsettled, although dopaminergic overactivity (Randrup & Munkvad, 1972) is still the most well known hypothesis. On the other hand, it is generally accepted that dopamine-releasing drugs like amphetamine can cause anxiety and hallucinations (Connell, 1958; Angrist & Sudilovsky, 1978). In fact, Silverstone & Goodall (1985) found that the anxiety caused by amphetamine is probably mediated through increased dopaminergic neurotransmission. Hence if acute dystonia caused transient recurrence of auditory hallucinations by increasing patients' anxiety, the mediating mechanism was probably dopaminergic overactivity.

The third possibility is that a common factor caused both acute dystonia and transient recurrence of auditory hallucinations. Despite criticisms and proposals of alternative hypotheses (Dinan, 1987), the dopamine hypothesis of neuroleptic action has survived (Iversen, 1987; Crow, 1987). Hence this common factor is likely to be a change in dopaminergic neurotransmission. A transient increase in dopaminergic neurotransmission following initial administration of neuroleptics is known to occur from studies of homovanillic acid in cerebrospinal fluid (Bowers, 1973; Fyro *et al*, 1974; Sedvall *et al*, 1974) and plasma (Harris *et al*, 1984). As pointed out above, only two hypotheses on the mechanism of acute dystonia have been proposed – increased or decreased dopaminergic neurotransmission. Even though dopaminergic overactivity is not universally accepted as the mediating mechanism of auditory hallucinations, dopaminergic underactivity has never been proposed as a mechanism. Thus dopaminergic overactivity might be the mediating mechanism. However, if this is so, it remains difficult to explain the observed response of both the dystonia and the hallucinations to anticholinergic drugs, and also the reported prompt relief of acute dystonia to parenteral methylphenidate, a dopaminergic agonist (Fann, 1966).

Why only a small number of patients experience acute dystonia on initial administration of neuroleptics is not known (Grohmann *et al*, 1983). Garver *et al* (1976) have suggested that a pharmacokinetic component may be involved. As dystonia occurs in 2–10% of patients receiving neuroleptics (Swett, 1975), it is surprising that the present author cannot find other reports of such transient recurrence of psychotic symptoms in the literature. Probably most patients already have active psychotic symptoms when they are put on neuroleptics, and hence transient exacerbation of such symptoms during acute dystonia is easily overlooked.

It should be pointed out that the neurochemical mechanism suggested above is only speculative, and is derived from clinical observation only – direct experimental evidence is lacking. Yet this proposed mechanism has much clinical importance because it implies that the psychotic symptoms during acute dystonia should be treated with anticholinergics, rather than with a further increase of neuroleptics. Furthermore, these symptoms should be prevented by changing to low-potency rather than high-potency neuroleptics. Finally, it is advisable to start patients on a low initial dose of antipsychotics or a test dose of depot injection (Mackay, 1982), to spare patients the physical discomfort of acute dystonia, and a transient exacerbation of psychotic symptoms.

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References

Angrist, B. & Sudilovsky, A. (1978) Central nervous system stimulants: historical aspects and clinical effects. In *Handbook of Psychopharmacology* (eds L. L. Iverson, S. D. Iverson & S. H. Snyder), vol. 11, pp. 99–165. New York: Plenum Press.

Borison, R. L., Blowers, A. J. & Diamond, B. I. (1982) New horizons in the treatment of neuropsychiatric disorders. In *Tardive Dyskinesia and Related Involuntary Movement Disorders* (ed. J. De Veaugh-Geiss), pp. 131–146. Boston: John Wright.

Bowers, M. B., Jr (1973) 5-Hydroxyindoleacetic acid (5HIAA) and homovanillic acid (HVA) following probenecid in acute psychotic patients treated with phenothiazines. *Psychopharmacologia*, **28**, 309–318.

Connell, P. H. (1958) *Amphetamine Psychosis* (Maudsley monographs). London: Oxford University Press.

Cooklin, R., Sturgeon, D. & Leff, J. (1983) The relationship between auditory hallucinations and spontaneous fluctuations of skin conductance in schizophrenia. *British Journal of Psychiatry*, **142**, 47–52.

Crow, T. J. (1987) The dopamine hypothesis survives, but there must be a way ahead. *British Journal of Psychiatry*, **151**, 460–465.

Dinan, T. G. (1987) Calcium-activated potassium conductance: an alternative to the dopamine hypothesis of neuroleptic action? *British Journal of Psychiatry*, **151**, 455–459.

Fahn, S. & Marsden, C. D. (1987) The treatment of dystonia. In *Movement Disorders 2* (eds C. D. Marsden & S. Fahn), pp. 359–382. London: Butterworths.

Fann, W. E. (1966) Use of methylphenidate to counteract acute dystonic effects of phenothiazines. *American Journal of Psychiatry*, **122**, 1293–1294.

Fyro, B., Wode-Helgodt, B., Borg, S., *et al* (1974) The effect of chlorpromazine on homovanillic acid levels in cerebrospinal fluid of schizophrenic patients. *Psychopharmacologia*, **35**, 287–294.

Garver, D. L., Davis, J. M., Dekirmenjian, H., *et al* (1976) Pharmacokinetics of red blood cell phenothiazine and clinical effects: acute dystonic reactions. *Archives of General Psychiatry*, **33**, 862.

Grohmann, R., Gunther, W. & Ruther, E. (1983) Adverse effects of psychotropic drugs. In *Psychopharmacology 1. Part 2: Clinical Psychopharmacology* (eds H. Hippius & G. Winokur), pp. 378–397. Amsterdam: Excerpta Medica.

Harris, P. Q., Brown, S. J., Friedman, M. J., *et al* (1984) Plasma drug and homovanillic acid levels in psychotic patients receiving neuroleptics. *Biological Psychiatry*, **19**, 849–860.

Hirsch, S. R. (1982) Medication and physical treatment of schizophrenia. In *Handbook of Psychiatry, vol. 3. Psychoses of Uncertain Aetiology* (eds J. K. Wing & L. Wing), pp. 74–87. Cambridge: Cambridge University Press.

Hollister, L. E. (1983) *Clinical Pharmacology of Psychotherapeutic Drugs* (2nd edn), pp. 110–171. New York: Churchill Livingstone.

Iversen, L. L. (1987) Commentary on Dinan's hypothesis. *British Journal of Psychiatry*, **151**, 459–460.

Korczyn, A. D. & Goldberg, G. J. (1972) Intravenous diazepam in drug-induced dystonic reactions. *British Journal of Psychiatry*, **121**, 75–77.

Loudon, J. B. (1983) Drug treatments. In *Companion to Psychiatric Studies* (3rd edn) (eds R. E. Kendell & A. K. Zealley), pp. 603–627. Edinburgh: Churchill Livingstone.

Mackay, A. V. P. (1982) Antischizophrenic drugs. In *Drugs in Psychiatric Practice* (ed. P. J. Tyrer), pp. 42–81. London: Butterworths.

Randrup, A. & Munkvad, I. (1972) Evidence indicating an association between schizophrenia and dopaminergic hyperactivity in the brain. *Orthomolecular Psychiatry*, **1**, 2–7.

Roos, R. A. C. & Bruyn, G. W. (1986) Symptomatic dystonias. In *Handbook of Clinical Neurology, vol. 5 (49): Extrapyramidal Disorders* (eds P. J. Vinken, G. W. Bruyn & H. L. Klawans), pp. 541–547. Amsterdam: Elsevier Science Publishers.

Roos, R. A. C. & Buruma, O. J. S. (1984) Extrapyramidal side effects of neuroleptic drugs. *Journal of Drug Therapy and Research*, **9**, 82–85.

Sedvall, G., Fyro, B., Nyback, H., *et al* (1974) Mass fragmentometric determination of homovanillic acid in lumbar cerebrospinal fluid of schizophrenic patients during treatment with antipsychotic drugs. *Journal of Psychiatric Research*, **11**, 75–80.

Silverstone, T. & Goodall, E. (1985) How amphetamine works. In *Psychopharmacology: Recent Advances and Future Prospects* (ed. S. D. Iverson), pp. 315–325. Oxford: Oxford University Press.

Silverstone, T. & Turner, P. (1982) *Drug Treatment in Psychiatry*, pp. 93–133. London: Routledge & Kegan Paul.

Slade, P. D. (1972) The effects of systemic desensitisation on auditory hallucinations. *Behaviour Research and Therapy*, **10**, 85–91.

Smith, M. J. & Miller, M. M. (1961) Severe extrapyramidal reactions to perphenazine treated with diphenhydramine. *New England Journal of Medicine*, **264**, 396–397.

Swett, C. (1975) Drug-induced dystonia. *American Journal of Psychiatry*, **132**, 532–534.

Walker, J. I. & Cavenar, J. O., Jr (1983) Hallucinations. In *Signs and Symptoms in Psychiatry* (eds J. O. Cavenar, Jr & H. K. H. Brodie), pp. 433–454. Philadelphia: Lippincott.

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Tardive Dystonia
The Benefits of Time

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Tardive dystonia is a rare movement disorder. We outline the development of tardive dystonia in a young schizopohrenic, and demonstrate the importance of applying a double-blind, placebo-controlled, cross-over trial of any putative successful treatment.

Tardive dystonia, first described by Keegan & Rajput (1973), is rare. In a comprehensive compilation of 40 cases (Burke *et al*, 1982) males predominated, age of onset was younger than for tardive dyskinesia, and response to treatment was poor. Tardive dystonia produces more severe functional handicap than tardive dyskinesia (Gimenez-Roldan *et al*, 1985). Case reports have suggested response to tetrabenazine, trihexphenidyl, and bromocriptine (Burke *et al*, 1982; Wolf & Koller, 1985; Luchins & Goldman, 1985), but there is no consensus on treatment. We outline the development and management of severe tardive dystonia in a schizophrenic patient.

Case report

This male patient was diagnosed as having schizophrenia in 1980, aged 20 years, on presentation with a three-month history of incongruity of affect, thought disorder, delusions of self-reference, and persecution and thought insertion. He was born prematurely and had two anoxic episodes shortly after birth. At nine months, epilepsy developed which was treated with phenobarbitone until the age of 12 years, since when he has only had occasional fits. He responded well to chlorpromazine, but developed pseudo-Parkinsonism, alleviated by orphenadrine. He remained on chlorpromazine (50 mg t.i.d.) and orphenadrine (50 mg t.i.d.) for the next four years, until relapsing in July 1984, when, in addition, he commenced fluphenazine decanoate (25 mg i.m.) every two weeks.

In February 1985 his family noticed excessive tongue movements. A reduction in chlorpromazine dose did not improve this. In April 1985 orphenadrine was increased to 100 mg t.i.d., followed by marked deterioration. The dyskinetic tongue movements were now associated with facial grimacing, writhing movements of hands and arms, and jerky movements of the neck to the left. In August 1985 all medication was discontinued; marked dystonia developed. His neck was pulled painfully and almost constantly to the left. There was frequent, sustained grimacing, affecting particularly the lower facial muscles on the left side, and also persistent protrusion of his tongue. A compensatory movement of the right hand up to his chin occasionally occurred. Severe functional handicap occurred, with difficulties in eating, drinking, talking, and walking. At that time his movements were thought to be due to hysteria.

However, his movements persisted, and in December 1985 he was first referred to one of us (SJC), and commenced diazepam (10 mg b.d.) and tetrabenazine (25 mg b.d.), with mild, sustained improvement in the choreic limb movements and dystonia. Wilson's disease was excluded, computerised tomography was normal, and EEG revealed a focus of left temporal spike waves. After three weeks diazepam was stopped, but there appeared to be a paradoxical response to tetrabenazine. The neck dystonia improved when the dose of tetrabenazine was increased, but this was limited by development of marked sialorrhoea. Reduction in dose of tetrabenazine or addition of orphenadrine exacerbated both dystonia and dyskinesia. In May 1986, because of failure to see further improvement, propranolol (160 mg q.i.d.) was commenced, in addition to tetrabenazine (12.5 mg *mane*, 25 mg *nocte*), with an apparent marked improvement in both types of abnormal movement. To assess the efficacy of propranolol more rigorously, we began a double-blind, cross-over study, comparing it with placebo.

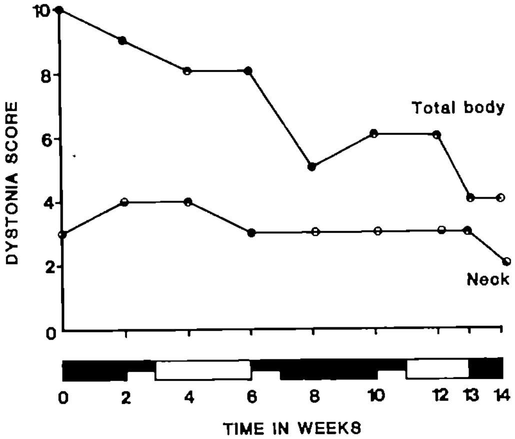

FIG. 1. The scores for dystonic movements as assessed by the modified AIMS. Medication during the double-blind cross-over study is indicated on the horizontal axis. Tetrabenazine was continued during the study. (■ propranolol; □ placebo; ■ cross-over.)

Double-blind cross-over study

Treatment alternated between matching capsules of propranolol (160 mg q.i.d.) (Imperial Chemical Industries, PLC) and placebo capsules (q.i.d.) for varying periods of up to three weeks, with an intervening week, during which the dose of propranolol was gradually increased or reduced (see Fig. 1). The patient remained on tetrabenazine (12.5 mg *mane*, 25 mg *nocte*) throughout. Mental state and extrapyramidal symptoms (EPS) were rated fortnightly, blind to medication (by MMD), using respectively the Manchester scale (Krawiecka *et al*, 1977) and the Simpson & Angus (1970) scale. A fortnightly video recording was made of his movements, and at the end of the 14-week study the videotapes were shown in random order, and rated blind for date by two raters (SJC and DJK) who reached an agreed rating for dyskinesia and dystonia. Tardive dyskinesia was assessed using the Abnormal Involuntary Movements Scale (AIMS; National Institute of Mental Health, 1976) and tardive dystonia using a modified AIMS (see Appendix). During the study no change was noted in clinical symptoms or ratings of EPS or tardive dyskinesia. Dystonia ratings are shown in Fig. 1.

Discussion

This case demonstrates how functionally handicapping tardive dystonia can be, and how increase in dose of anticholinergic medication may precipitate it. This paradoxical response, compared with that for acute dystonia, is akin to the pattern seen in other tardive movement disorders, such as tardive dyskinesia and tardive akathisia (Braude & Barnes, 1983). The earliest sign in this patient was jerking movements of the neck, and this has been reported for other dystonias. It should also be noted that his movements were initially thought to have an hysterical basis. Lesser & Fahn (1978) noted misdiagnosis of idiopathic torsion dystonia as hysterical conversion reaction in 37 of 84 patients.

The study does not demonstrate consistent change in dystonia scores with change from propranolol to placebo and vice versa. Although the greatest improvement occurred around weeks 7 and 8 following change from placebo to propranolol, deterioration occurred between weeks 8 and 10 during propranolol treatment. Further, the next greatest improvement was during a placebo phase (week 13). Change from propranolol to placebo never resulted in deterioration. Thus our initial clinical impression of marked improvement with propranolol was not borne out. It is perhaps worth emphasising that in uncommon disorders, placebo-controlled studies, in single cases, ought to be carried out more often to substantiate claims for dramatic response to certain treatments.

There is no doubt that during the initial period of treatment in 1986, before commencement of propranolol, tetrabenazine produced a partial improvement in the dystonic symptoms. It is impossible to be sure whether or not continuation of tetrabenazine was responsible for the gradual response seen during the study period, because improvement following the initial response to it had reached a plateau. Subsequently, we have been able to discontinue all medication, and have seen further gradual disappearance of the abnormal movements.

Appendix

The modified AIMS for dystonia consisted of assessing the patient for each of the seven body areas, as described on the AIMS for dyskinesia, and scoring from 0 to 4 for each area, depending on the severity of the dystonic movements. The same criteria of 'questionable', 'mild', 'moderate', and 'severe' were employed.

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References

BRAUDE, W. M. & BARNES, T. R. E. (1983) Late onset akathisia: an indicant of covert dyskinesia: two case reports. *American Journal of Psychiatry*, **140**, 611–612.

BURKE, R. E., FAHN, S., JANKOVIC, J., *et al* (1982) Tardive dystonia: late onset and persistent dystonia caused by antipsychotic drugs. *Neurology (NY)*, **32**, 1335–1346.

GIMENEZ-ROLDAN, S., MATEO, D. & BARTOLOME, P. (1985) Tardive dystonia and severe tardive dyskinesia. *Acta Psychiatrica Scandinavica*, **71**, 488–494.

KEEGAN, D. L. & RAJPUT, A. H. (1973) Drug induced dystonia tarda treatment with L-dopa. *Diseases of the Nervous System*, **38**, 167–169.

KRAWIECKA, M., GOLDBERG, D. & VAUGHN, M. (1977) A standardised psychiatric assessment scale for rating chronic psychotic patients. *Acta Psychiatrica Scandinavica*, **55**, 299–308.

LESSER, R. P. & FAHN, S. (1978) Dystonia: a disorder often misdiagnosed as a conversion reaction. *American Journal of Psychiatry*, **135**, 349–352.

LUCHINS, D. J. & GOLDMAN, M. (1985) High dose bromocriptine in a case of dystonia. *Biological Psychiatry*, **20**, 179–181.

NATIONAL INSTITUTE OF MENTAL HEALTH (1976) Abnormal Involuntary Movements Scale (AIMS). In *ECDEU Assessment Manual* (ed. W. Guy), pp. 534–537. Rockville, Maryland: US Department of Health, Education and Welfare.

SIMPSON, G. M. & ANGUS, J. W. S. (1970) A rating scale for extrapyramidal side effects. *Acta Psychiatrica Scandinavica (suppl.)*, **212**, 11–19.

WOLF, M. E. & KOLLER, W. C. (1985) Tardive dystonia: treatment with trihexphenidyl. *Journal of Clinical Psychopharmacology*, **5**, 247–248.

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Obsessive–Compulsive Disorder in a Mentally Retarded Woman

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Obsessive–compulsive disorder is extremely rare among mentally retarded people. We report here a case of a mildly mentally retarded woman who exhibits contamination obsessions, compulsive hand-washing rituals, and avoidance.

Obsessive–compulsive disorder (OCD) is extremely rare among mentally retarded people (Novosel, 1984; McNally & Ascher, 1987). Although 'compulsive' stereotypical behaviour (e.g. body rocking) is common in this population, it is clearly distinguishable from compulsive rituals triggered by anxiety-based obsessions (Rachman & Hodgson, 1980, p. 96). Indeed, as Matson (1982) notes, many clinicians doubt whether OCD occurs in persons with subnormal intelligence. Consistent with the notion that intellectual handicap protects against OCD, obsessive–compulsives often have above average intelligence (Rasmussen & Tsuang, 1984).

Matson (1982) published the only detailed report of OCD in mentally retarded people. He treated three mildly retarded men whose concerns with personal tidiness led them repeatedly to check their clothes and personal appearance, which interfered with their performance in a sheltered workshop. Treatment included exposure to situations that triggered checking, differential positive reinforcement for not checking, modelling of appropriate on-task behaviour, performance feedback, and overcorrection for violations of response prevention of rituals. Treatment reduced checking and self-reports of anxiety.

We describe here a mentally retarded woman with OCD. She had been discharged from our facility and was living in a group home when we obtained permission from her legal guardian to interview her.

Case report

Ms D is a 51-year-old single, white woman with mild mental retardation of unknown aetiology (WAIS-R full scale IQ = 54). She lives in a group home for mentally retarded people, and attends a work activity centre.

Ms D is the oldest of three children born to Scottish immigrants to the USA. Of her two sisters, the older is intellectually gifted, whereas the younger is mildly retarded. Except for her alcoholic grandfathers, there is no family history of psychopathology.

Ms D's records indicate an uncomplicated, full-term birth following a 12-hour labour. At six weeks of age, she developed a high fever requiring her admission to hospital. No further information was available regarding this illness. She began to walk at 13 months, and to talk when three and a half years old. Her language delay prompted an evaluation, resulting in a medical diagnosis of mental retardation. Ms D's formal education was terminated after her first day at school because of the severity of her tantrums. According to her mother, Ms D became anxious before school age whenever deviations from the family routine occurred (e.g. changes in seating arrangements at the dinner table). When anxious, Ms D would compulsively arrange objects.

When eight years old, Ms D was institutionalised at a state school for the mentally handicapped. According to her mother, Ms D's 'mental problems' made her unmanageable at home. These problems ranged from disruptiveness to mutism, which lasted three months. Institutional records describe Ms D's social withdrawal, periodic polydipsia, and hoarding of various objects. Her OCD emerged during early adolescence, and has remained essentially unchanged for the past 35 years. In response to contamination obsessions triggered by 'dirty' objects, she would compulsively wash her hands and face, sometimes for hours. She always carried a towel to decontaminate herself should she become dirty. When asked why she washed so much, Ms D would cry out, "Clean! Clean! I want to be clean! I don't want to be dirty!"

When 42 years old, Ms D was transferred to a smaller state facility, where efforts to reduce her obsessive–compulsive behaviour began. She received amitriptyline with little benefit. Several behaviour-modification procedures were implemented that produced minimal change in her OCD symptoms. She participated in a token economy on her living unit, where she received positive reinforcement for completing pre-vocational tasks, and for appropriate socialisation with peers. She also received tokens for refraining from ritualising for specified periods of time (differential reinforcement of other behaviour), and was fined tokens for engaging in compulsive rituals (response cost). Graduated exposure *in vivo*, consisting of having staff stand near her and touch her appropriately (e.g. attempts to shake hands) was ineffective. She also failed to benefit from progressive muscle relaxation. Physical attempts to prevent excessive hand-washing produced extreme anxiety, and the patient would hit herself and bang her head. Thioridazine (25 mg t.i.d.) reduced the severity of her rituals somewhat.

When 50 years old, Ms D was transferred to a community residential home for mentally retarded adults, where she was observed and interviewed by the authors. Currently she is particularly obsessed about contamination from other people. For example, when one of us extended his hand to shake hers, she became visibly anxious, recoiling and crying out that he was 'dirty'. She became increasingly anxious during the interview, and eventually ran into the bathroom to wash her hands. Interestingly, she did not respond to objects we had touched as dirty. Hence, 'contamination' did not generalise as easily as it often does for obsessive–compulsives of normal intelligence.

Although staff members report a high frequency of hand-washing, washing episodes now last only about ten seconds. Indeed, she limits her ritualising through avoidance. She minimises contact with objects by grasping them with her thumb and fingertips, and holds her hands close to her chest to prevent contact with contaminants.

Ms D takes a daily 30-minute shower, during which she washes herself in the same sequence. If her shower is interrupted, say, by a staff member calling to her, she becomes anxious and begins all over again.

Her OCD has prevented her from making friends, as she maintains a physical distance from others. Although she attends a work activity centre during the day, her productivity is minimal.

Discussion

Ms D exhibits classic OCD. Perhaps due to her limited intelligence, she does not exhibit any apparent subjective resistance to her obsessions and compulsions, nor does she seem aware that her behaviour is abnormal.

Behavioural treatment with mentally retarded obsessive–compulsives is likely to be difficult if they do not recognise the abnormality of their behaviour, and if they do not wish to overcome their fears. As exemplified by the present case, non-compliance undermines exposure and response prevention treatments that are otherwise highly effective (for a review, see Marks, 1987). Perhaps such patients would respond to clomipramine (Christensen *et al*, 1987) or fluvoxamine (Perse *et al*, 1987), either alone or in combination with behaviour therapy.

References

CHRISTENSEN, H., HADZI-PAVLOVIC, D., ANDREWS, G., *et al* (1987) Behavior therapy and tricyclic medication in the treatment of obsessive–compulsive disorder: a quantitative review. *Journal of Consulting and Clinical Psychology*, **55**, 701–711.

MARKS, I. M. (1987) *Fears, Phobias, and Rituals*. New York: Oxford University Press.

MATSON, J. L. (1982) Treating obsessive–compulsive behavior in mentally retarded adults. *Behavior Modification*, **6**, 551–567.

MCNALLY, R. J. & ASCHER, L. M. (1987) Anxiety disorders in mentally retarded people. In *Anxiety and Stress Disorders: Cognitive-Behavioral Assessment and Treatment* (eds L. Michelson & L. M. Ascher), pp. 379–394. New York: Guilford.

NOVOSEL, S. (1984) Psychiatric disorder in adults admitted to a hospital for the mentally retarded. *British Journal of Mental Subnormality*, **30**, 54–58.

PERSE, T. L., GREIST, J. H., JEFFERSON, J. W., *et al* (1987) Fluvoxamine treatment of obsessive–compulsive disorder. *American Journal of Psychiatry*, **144**, 1543–1548.

RACHMAN, S. J. & HODGSON, R. J. (1980) *Obsessions and Compulsions*. Englewood Cliffs: Prentice-Hall.

RASMUSSEN, S. A. & TSUANG, M. T. (1984) The epidemiology of obsessive–compulsive disorder. *Journal of Clinical Psychiatry*, **45**, 450–457.

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Mania in a Five-Year-Old Child with Tuberous Sclerosis

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A five-year-old girl presented with mania and adenoma sebaceum. Later she developed grand mal seizures, and EEG revealed a prominent right temporal focus. It is important to consider tuberous sclerosis as aetiologically related to mood disorders.

Tuberous sclerosis is a rare disease, of varied clinical presentation. Besides the classic triad of mental retardation, seizures, and adenoma sebaceum, other common features include retinal phacoma, 'shagreen patches' on the trunk, and 'ash-leaf patches' on the trunk or limbs (Adams & Victor, 1985). Atypical cases, lacking one or more components of the triad, may be quite common (Duvoisin & Vinson, 1961).

Psychotic manifestations are frequently seen in patients with tuberous sclerosis (Clarke, 1987), and Critchley & Earl (1932) described a "primitive type of catatonic schizophrenia" as an essential feature. There have been reports of tuberous sclerosis presenting with autistic behaviour (Mansheim, 1979; Lawlor & Maurer, 1987). We report tuberous sclerosis in a girl who presented with mania.

Case report

MK, a five-year-old tribal girl was brought for psychiatric consultation by her parents with a three-month history of sustained cheerfulness, overactivity, excessive friendliness, and occasional abusiveness. She was talking much more than usual. She would accost strangers on the road, and talk to them, sing songs, and ask them for sweets and presents in return. She was also very distractible. She would leave home at odd hours, and her mother had frequently to restrain her physically. She asked for food at very short intervals, and her total consumption was unusually high. At times she would become irritable and abusive.

MK is the second of two sibs. She was born of a non-consanguinous marriage, a full-term normal child, delivered at home. There were no pre-, peri- or post-natal complications. Her milestones were within the normal range, except for slight delay in the acquisition of speech. Her pre-morbid temperament was quiet and shy. She had no formal education because of the low socio-economic status of her parents. A few months before the onset of this illness, her parents had noticed reddish, pin-sized nodules on her nasolabial folds and cheeks. There had been no history of seizures.

There was no history of any neurological or psychiatric problems in the family, except for non-dependent abuse of alcohol by the father. No other family member had similar lesions on the face.

Examination revealed adenoma sebaceum, a large café-au-lait spot on the neck, and three ash-leaf patches on the legs. No other feature of tuberous sclerosis was present. Neurological examination was unremarkable. She did not show any clinical evidence of mental retardation. On mental state examination she was found to be abnormally cheerful, friendly, overtalkative, easily distractible, and overactive. She was domineering and demanding. Later she started hitting her mother, and even tore her dress when her demands were not immediately fulfilled.

Haloperidol (6 mg per day) was prescribed, and the parents were asked to bring her for weekly follow-up. However, the next consultation was after five weeks. The day before, she had lost consciousness, and there was flexion and extension of the limbs and trunk. Haloperidol had been given intermittently with slight improvement in behaviour. A skull X-ray and EEG were advised, and haloperidol stopped.

As she was not brought for follow-up over the next three months, her parents were contacted. It was found that one week after the first episode of loss of consciousness, she had had a generalised tonic-clonic seizure. Since then she had had many similar seizures, up to three a day. The maximum fit-free interval was one week. The behavioural symptoms persisted. One day, while jumping around in the kitchen, she had stepped on a piece of burning wood, and burnt her legs. There was no alteration of consciousness or seizure at the time of the accident. The wound had gradually healed.

The skull X-ray did not show any intracranial calcification or other abnormalities. Computerised tomography demonstrated tuberous sclerosis with subependymal calcifications along the lateral ventricles. EEG showed normal background activity with numerous sharp and slow-wave discharges with occasional spikes. There was a definite focus in the right temporal region, and another possible focus in the left frontal region. Her IQ indicated her to be mildly retarded.

Carbamazepine (200 mg per day) was started. Follow-up two weeks later showed distinct improvement in her behaviour. She had five to six abortive seizures during this period. The dose of carbamazepine was gradually increased to 400 mg per day. She had two further abortive seizures in one week and none thereafter; she was reported to have become more irritable, abusive, and demanding. As she was already on maximum carbamazepine doses (on a mg/kg body weight basis), and facilities for estimating levels of serum carbamazepine were not available, haloperidol in gradually increasing doses (up to 10 mg a day) was added. She has since shown remarkable improvement in her behavioural symptoms.

Discussion

The clinical features that the patient presented with meet Research Diagnostic Criteria (Spitzer *et al*, 1978) for a hypomanic episode. Mania during early childhood is thought to be extremely rare (Youngerman & Canino, 1978). To our knowledge this is the first reported case showing an association between mania and tuberous sclerosis. Considering the rarity of these conditions, their coinciding is extremely unlikely.

The concept of secondary mania was introduced by Krauthammer & Klerman (1978). DSM-III-R (American Psychiatric Association, 1987) lists such conditions under "Organic mood disorder". Besides the presence of affective symptoms, the diagnosis is based on "evidence, from the history, physical examination, or laboratory tests, of a specific organic factor that is judged to be etiologically related to the disturbance".

Many neurological, toxicological, and metabolic disorders have been associated with secondary mania (Cummings, 1986). Mania seems to be more common with right-sided than with left-sided lesions (Cummings, 1986). Rosenbaum & Barry (1975) reported a man who developed left-sided Jacksonian seizures becoming generalised after surgical damage to the right temporal lobe. EEG showed a right temporal focus. Three months after the onset of seizures he developed a hypomanic illness. Flor Henry (1969) reported that epilepsy of the non-dominant temporal lobe is associated with manic–depressive illness. Bear & Fedio (1977) reported that patients with right-sided foci showed significantly more elation and increased ratings of affective disturbance compared with those with left-sided foci. Thus a grossly abnormal EEG with frequent seizure discharges and a well-defined focus on the right temporal lobe would support the contention that the lesion of tuberous sclerosis is aetiologically related to the mood syndrome.

Secondary mania is generally associated with a late age of onset (Krauthammer & Klerman, 1978). Considering the rarity of mania in childhood, we suggest that occurrence of mania at either extreme of age should be viewed with suspicion, and all efforts should be made to determine whether the mania is secondary to organic dysfunction.

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References

Adams, R. D. & Victor, M. (1985) *Principles of Neurology*. New York: McGraw Hill.

American Psychiatric Association (1987) *Diagnostic and Statistical Manual for Mental Disorders* (3rd edn, revised) (DSM-III-R). Washington, DC: APA.

Bear, D. & Fedio, P. (1977) Quantitative analysis of interictal behaviour in temporal lobe epilepsy. *Archives of Neurology*, **34**, 454–467.

Clarke, B. J. (1987) Epilepsy and psychosis – ask the family. *British Journal of Psychiatry*, **150**, 702–703.

Critchley, M. & Earl, C. J. C. (1932) Tuberous sclerosis and allied conditions. *Brain*, **55**, 311–346.

Cummings, J. C. (1986) Organic psychoses: delusional disorders and secondary mania. *Psychiatric Clinics of North America*, **9**, 293–311.

Duvoisin, R. C. & Vinson, W. M. (1961) Tuberous sclerosis, report of three cases without mental defect. *Journal of the American Medical Association*, **175**, 869–873.

Flor Henry, P. (1969) Schizophrenic-like reactions and affective psychoses associated with temporal lobe epilepsy: etiological factors. *American Journal of Psychiatry*, **126**, 400–404.

Krauthammer, C. & Klerman, G. L. (1978) Secondary mania. *Archives of General Psychiatry*, **35**, 1333–1338.

Lawlor, B. A. & Maurer, R. G. (1987) Tuberous sclerosis and the autistic syndrome. *British Journal of Psychiatry*, **150**, 396–397.

Mansheim, P. (1979) Tuberous Sclerosis and Autistic Behaviour. *Journal of Clinical Psychiatry*, **40**, 97–98.

Rosenbaum, A. H. & Barry, M. J., Jr (1975) Positive therapeutic response to lithium in hypomania secondary to organic brain syndrome. *American Journal of Psychiatry*, **132**, 1072–1073.

Spitzer, R., Endicott, J. & Robins, E. (1978) Research diagnostic criteria. *Archives of General Psychiatry*, **34**, 773–782.

Youngerman, J. & Canino, I. A. (1978) Lithium carbonate use in children and adolescents. *Archives of General Psychiatry*, **35**, 216–224.

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Status Epilepticus after Electroconvulsive Therapy

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Status epilepticus is a rare complication of ECT. We describe a patient who suffered a prolonged seizure which required termination with intravenous diazepam. The status epilepticus was not accompanied by motor movements, and the diagnosis was made only because of simultaneous EEG monitoring. The incidence of status epilepticus after ECT may be underestimated.

Status epilepticus is a rare complication of electroconvulsive therapy (ECT). A literature search found only six reported cases of prolonged seizures with conventional ECT (Weiner, 1981; Prakash & Leavell, 1984; Peters *et al*, 1984; Kaufman *et al*, 1986). Prolonged seizures are more common after multiple monitored ECT (MMECT), where several seizures are induced at one session (Strain & Bidder, 1971; Bridenbaugh *et al*, 1972). Strain & Bidder (1971) noted that status epilepticus may be difficult to detect because motor activity may be slight and localised. Weiner *et al* (1980*a*) suggested that monitoring ECT by electroencephalogram (EEG) might reveal a higher incidence of prolonged seizures. We report a case of status epilepticus after ECT without motor manifestations. The diagnosis was made because the ECT was monitored by multichannel EEG.

Case report

A 29-year-old single female dentist was admitted to a general hospital in April 1988 after an overdose. She had liquidised approximately 200 paracetamol and 20 chlorpromazine tablets in whisky. She had swallowed this mixture 20 hours earlier, and then had injected herself subcutaneously with adrenaline. One month earlier she had been discharged from a psychiatric hospital after her episode of hypomania, which had been treated with chlorpromazine. She had no past history of parasuicide, nor any significant past medical history.

On admission, she was drowsy but orientated. The plasma paracetamol concentration was grossly elevated at 280 mg/l, but it was too late to institute any prophylaxis against liver damage. Over the next two days she became jaundiced, and lapsed into unconsciousness for two days. Her liver function was grossly deranged, her prothrombin time became prolonged, and she required treatment with fresh frozen plasma on two occasions. She made a slow but steady recovery, and was transferred to a psychiatric hospital two weeks later.

She still appeared jaundiced, but apparently recovering physically, and her liver function tests were almost normal. At first she was subdued but then obviously depressed. She was tearful and at times retarded, had difficulty sleeping, and ruminated on ideas of unworthiness. Gradually she became hopeless and, once more, suicidal. She was not prescribed any drugs.

One month after the overdose, she started a course of ECT. The anaesthetic consisted of 250 mg thiopentone followed by 50 mg suxamethonium intravenously. She was ventilated with oxygen for about a minute before electrical stimulation. She was treated by an Ectron CCX Series 3 machine (850 mA, 45 Hz, 1.5 ms, 5 s) with bilateral electrodes. She developed generalised tonic clonic muscle activity which was visible for 38 seconds. Thereafter she stopped moving, became flaccid, and did not breathe spontaneously.

ECT was monitored on six channels of a portable EEG machine. Before ECT, the record showed a normal alpha rhythm, which attenuated on eye opening. Within two seconds of electrical stimulation, the record showed high-amplitude spike and wave activity in all channels at a frequency of 4 Hz. This discharge continued long after motor activity had ceased. The patient remained flaccid and did not breathe spontaneously. She was ventilated satisfactorily by the anaesthetist, who was reluctant to administer an anticonvulsant drug in the absence of tonic clonic movements. After 10 minutes of seizure activity, she was given 5 mg diazepam intravenously. Over the next 30 seconds the spike and wave activity decreased in amplitude and in frequency. She began to move, and large slow waves with occasional muscle artefact appeared in all channels. The recording had to be discontinued when the patient was transferred to the recovery room.

After 45 minutes she walked back to the ward, where she was noted to be disorientated and unaware she had had ECT. Physical examination revealed no focal neurological signs, and her fundi were normal. She was generally hyper-reflexic, and both plantar responses were extensor.

Two hours later she was found on top of her bed, having a generalised tonic clonic convulsion involving all limbs. Simple resuscitation was performed and 10 mg diazepam was given intravenously, which successfully stopped the fit. Five minutes later, without having regained consciousness, she had a further tonic clonic convulsion. A further 10 mg diazepam was given intravenously.

She was transferred to a medical ward, where she was drowsy and uncoordinated. On physical examination she appeared jaundiced, was generally hyper-reflexic, and had extensor plantar reflexes. Liver function tests were still slightly elevated (bilirubin 107 mmol/l, alanine aminotransferase 99 U/l, alkaline phosphatase 136 U/l), and analysis of arterial blood gases revealed a slight respiratory alkalosis. Other investigations, including full blood count, erythrocyte sedimentation rate, prothrombin time, urea and electrolytes, glucose, chest X-ray, and electrocardiograph gave normal results. She was managed conservatively, and required no further anticonvulsant treatment. There were no further seizures during her medical admission. The next day she was more alert, able to carry out simple instructions, but was disorientated, and had difficulty with finding words. An apparent anterior dislocation of the left shoulder was reduced. Computerised tomography (CT) of the brain was normal. An EEG revealed an underlying rhythmical slow-wave activity, which was maximal in the left tempora region. This was compatible with a post-ictal record. Plasma pseudocholinesterase activity was found to be low at 0.45 units/ml (normal range, 2.6–7.8 units/ml), which may have been the result of liver damage. Dibucaine inhibition of pseudocholinesterase activity was reduced to 61%, which suggests she was heterozygous for a genetic variant of pseudocholinesterase (Miller, 1986). It is likely that the action of suxamethonium would have been ‘slightly prolonged’ during ECT (Miller, 1986).

One week after ECT, she returned to the psychiatri ward, still depressed. Later that day, she absconded from the ward. She was found the next morning by a railway line, having committed suicide by decapitation.

Discussion

Prolonged seizures after ECT may be associated with hyperoxygenation, cerebral hyperexcitability, and the use of MMECT (Weiner *et al*, 1980*a*). Antidepressant and neuroleptic drugs may also reduce the seizure threshold (Kaufman *et al*, 1986). Abnormal seizure activity has also been reported when ECT is combined with lithium carbonate (Weiner *et al*, 1980*b*), and theophylline (Peters *et al*, 1984). The aetiology of status epilepticus in this case is unclear.

The anaesthetic procedure was standard, there was no past history of seizures, and the patient had not received any drugs within one month of ECT. It may be that the patient suffered a small cerebral haemorrhage when her clotting time was abnormally prolonged; if so, this was not apparent on physical examination or on CT. The range of electrical stimulus necessary to induce a seizure in brief-pulse ECT is wide, and young women are at the low end of this range (Sackeim *et al*, 1987). It may be that this young woman had an unusually low seizure threshold.

Although the aetiology of the status epilepticus is uncertain, it is clear that the diagnosis and treatment of this complication would have been delayed in the absence of simultaneous EEG monitoring. We wonder how many prolonged seizures have been missed, and mistaken for unusual reactions to an anaesthetic drug or severe post-ictal states (Weiner *et al*, 1980*a*), or spontaneous second seizures (James & Simpson, 1984).

It is likely that prolonged seizures can be tolerated without the risk of ischaemic brain damage as long as the patient is adequately oxygenated and relaxed (Weiner, 1984). However, prolonged seizures have no therapeutic advantage (Strain & Bidder, 1971), and may be associated with confusion and amnesia. Convulsive status epilepticus is best terminated without delay, as it has a risk of locomotor injury; this patient suffered a dislocated shoulder. Intravenous diazepam (5–10 mg) is usually effective (Bridenbaugh *et al*, 1972), although up to 30 mg may be required.

Status epilepticus after ECT is not a contraindication to further ECT, although MMECT is best avoided. Weiner (1981) and Kaufman *et al* (1986) have reported four cases where further ECT was given with prophylaxis by anticonvulsant drugs. Prophylaxis with phenytoin may necessitate the use of an increased electrical stimulus, and the seizure threshold may be raised above the maximum output of certain ECT machines. Carbamazepine prophylaxis may be satisfactory, without the need for the marked increase in stimulus intensity.

References

BRIDENBAUGH, R. H., DRAKE, F. R. & O'REYAN, T. J. (1972) Multiple monitored electroconvulsive treatment of schizophrenia. *Comprehensive Psychiatry*, **13**, 9–17.

JAMES, A. & SIMPSON, D. (1984) Spontaneous second fit after ECT. *British Journal of Psychiatry*, **145**, 337–338.

KAUFMAN, K. R., FINSTEAD, B. A. & KAUFMAN, E. R. (1986) Status epilepticus following electroconvulsive therapy. *Mount Sinai Journal of Medicine*, **53**, 119–122.

MILLER, R. D. (1986) *Anesthesia* (2nd edn), vol. 2, pp. 917–918. Edinburgh: Churchill Livingstone.

PETERS, S. G., WOCHOS, D. N. & PETERSON, G. C. (1984) Status epilepticus as a complication of concurrent electroconvulsive and theophylline therapy. *Mayo Clinic Proceedings*, **59**, 868–870.

PRAKASH, R. & LEAVELL, S. R. (1984) Status epilepticus with unilateral ECT: a case report. *Journal of Clinical Psychiatry*, **45**, 403–404.

SACKEIM, H., DECINA, P., PROHOVNIK, I., *et al* (1987) Seizure threshold in electroconvulsive therapy. *Archives of General Psychiatry*, **44**, 355–360.

STRAIN, J. J. & BIDDER, T. G. (1971) Transient cerebral complication association with multiple-monitored electroconvulsive therapy. *Diseases of the Nervous System*, **32**, 95–100.

WEINER, R. D. (1981) ECT-induced status epilepticus and further ECT: a case report. *American Journal of Psychiatry*, **138**, 1237–1238.

—— (1984) Does electroconvulsive therapy cause brain damage? *Behavioural and Brain Sciences*, **7**, 1–54.

——, VOLOW, M. R., GIANTURCO, D. T., *et al* (1980*a*) Seizures terminable and interminable with ECT. *American Journal of Psychiatry*, **137**, 1416–1418.

——, WHANGER, A. D., ERWIN, W., *et al* (1980*b*) Prolonged confusional state and EEG seizure activity following concurrent ECT and lithium use. *American Journal of Psychiatry*, **137**, 1452–1453.

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Contents: Family therapy for schizophrenia/Better to be depressed in Australia . . ./. . . or not?/AIDS hypochondriasis/Journal contents page/Obstetric liaison/Calcium techniques/Neuroleptic malignant syndrome/NMS and thioxanthenes/Schizophrenia, season of birth and maternal age/Homosexual erotomania/Post-traumatic stress disorder/Neuronal misconceptions/Unreliable urine samples/Munchausen's syndrome by proxy/Sorcery and psychiatry/Solvent abuse psychosis.

Family therapy for schizophrenia

SIR: Leff *et al* (*Journal*, January 1989, **154**, 58–66) recommend establishing relatives' groups, in conjunction with family education and one or more initial family therapy sessions in the home, as the most cost-effective and efficient management of schizophrenic patients maintained on neuroleptic medication and living in contact with relatives having high expressed emotion (EE).

Before incorporating this recommendation into routine clinical practice, several questions need to be addressed. The results of the two-year follow-up were not entirely clearcut, since 2 of 12 patients in the experimental group committed suicide. Professor Leff *et al* do not report on the long-term follow-up of their first trial of intervention. This data seems essential before concluding that intensive social interventions are really cost-effective, given the considerable demand on professional resources.

Professor Leff *et al* refer to difficulty in accumulating sufficient families. Could they elaborate? Our own research on the course and outcome of first lifetime episode schizophrenia suggests that at this stage of the disorder, parents are not prepared to consider family therapy (independent of EE status), but are prepared to participate in relatives' groups in conjunction with family education and participation in planning rehabilitation (Waring *et al*, 1988). Our experience suggests a lack of efficiency in accumulating sufficient families for family therapy at this early stage of the disorder. An alternative explanation is that the process of engagement of these families requires more than "tact and patience", and perhaps skills that "ordinary" clinicians, not involved in high profile research projects, do not possess. We are aware of very few clinical psychiatrists who in their treatment of schizophrenia are able to combine educational, behavioural, structural, and systemic techniques of family therapy.

One other explanation of our "low efficiency" is that the high EE families studied by Professor Leff *et al* are unusually co-operative and compliant in participating in a family therapy package. A young person with a first episode of schizophrenia is fortunate to have a family who are considerate and tolerant. This attitude of concern appears to be independent of the EE status of the family or whether or not they are treated with social interventions (Johnstone *et al*, 1986; McCreadie *et al*, 1987).

We would also appreciate a clarification of what exactly Professor Leff *et al* mean by "face to face" contact. Does it refer to a patient and a relative being in the home at the same time? Our experience suggests that few adolescent schizophrenics interact directly with relatives for five hours a day. Perhaps another term would be more helpful?

Finally, the programme recommended appears to have provided family therapy to only six families per year! Is it possible that the treatment effectiveness reflects an alteration of parental attitude from fear and hostility towards a child's perceived deviant behaviour to an attitude of compassion and sympathy for a child with a "broken brain"? If so, it is not surprising that, for the short term, a family can express tolerance towards a schizophrenic child.

We greatly admire the research of Professor Leff *et al*. Our question is whether, and how, to transfer family therapy approaches from 'select' research samples of patients and their compliant families to the vast majority of out-patient schizophrenics seen in day-to-day clinical practice.

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References

JOHNSTONE, E. C., CROW, T. J., JOHNSON, A. L. *et al* (1986) The Northwick Park Study of First Episodes of Schizophrenia. *British Journal of Psychiatry*, **148**, 115–120.

Scottish Schizophrenia Research Group (1987) The Scottish First Episode Schizophrenia Study. *British Journal of Psychiatry*, **150**, 331–333.

WARING, E. M., LEFCOE, D. H., CARVER, C. *et al* (1988) The course and outcome of early schizophrenia. *Psychiatric Journal of the University of Ottawa*, **13**, 194–197.

SIR: Dr Waring *et al* raise a number of questions about our attempts to help the families of schizophrenic patients. We have not followed up our two trials beyond two years. Although we recognise the importance of a longer perspective, it is difficult to maintain control over the interventions received beyond two years. For the same reason, it is rare for trials of maintenance drugs to exceed this period. Uncontrolled follow-ups are of doubtful value; however, we did maintain contact with a number of families for three years or more and did not learn of any further suicides. Moreover, there were no suicides in our second trial, which may reflect improved intervention techniques, or merely better luck. With regard to the demand on professional resources, this is maximal during the first year of intervention for most families. Beyond that, families appreciate having access to professional help from time to time, but in many cases a phone call or letter once a month or less is sufficient.

Our difficulty in accumulating sufficient families was not due to their reluctance to accept the help offered, but to our stringent entry criteria for the trials. We focused on the highest risk families; those in which patients were in high face-to-face contact (more that 35 hours per week in the *same room* as the relative) with high EE relatives. These constitute no more than 1 in 6 of all schizophrenic admissions. We recognize the limitation this imposes on generalising our findings to "the vast majority of outpatient schizophrenics seen in day-to-day clinical practice", and have never claimed that our recommendations extend to all patients living with families. Indeed, the study of the Scottish Schizophrenia Research Group (1987) reveals that for patients living with relatives in a rural community, the prognosis for schizophrenia is remarkably good, only 19% being readmitted in the course of a year.

Our recommendations apply, not to these fortunate individuals, but to the high-profile patients who are frequently readmitted despite receiving drug therapy. We are therefore less concerned with the first onset patients that Dr Waring *et al* are attempting to help, although we do attempt to engage their families if they are high EE, high contact. We have not experienced any insuperable obstacles to this, perhaps because we begin the process of engagement by offering knowledge about the illness, for which relatives are eager, and follow on by attempting "to help the family to help the patient". We never target the family as the object of "therapy". An additional factor which facilitates engagement is our readiness to make home visits to those families who are unwilling or unable to come to us.

It is our view that reduction in high-EE attitudes does represent an increase in tolerance and understanding for the sufferer. However, this is also accompanied by significant changes in the coping behaviour employed by relatives. We are in the process of studying these in more detail.

Finally, we share the concern of Dr Waring *et al* that our intervention techniques may be perceived as beyond the capability of ordinary clinical teams. This has impelled us to study whether the techniques can be learned and effectively applied by psychiatric nurses in a routine clinical service. We shall report on this research in the fullness of time.

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Better to be depressed in Australia . . .

SIR: Kiloh *et al* (*Journal*, December 1988, **153**, 752–757) describe better outcome after 18 years among New South Wales depressives than among our Maudsley patients (Lee & Murray, 1988). They suggest that the poorer outcome in London may have been due to the mis-inclusion of schizophrenic and schizoaffective cases, and are inclined to dismiss our findings concerning the predictive power of the neurotic-psychotic continuum on similar grounds.

We have re-analysed our data after excluding all those patients who developed schizophrenia and schizoaffective disorder: 25% of the remainder still fell into the operationally defined poor-outcome group. We further examined whether the presence of delusion, hallucinations, or mood incongruent features during the index admission predicted poor outcome. None of these indicators of possible "mis-inclusion" were correlated with poor outcome. Finally, and most surprisingly, we found that the development of schizophrenia or schizoaffective disorder was not associated with higher ('psychotic') scores on the neurotic-psychotic continuum at the time of the index admission. Thus position on the continuum did predict poor outcome, but not by identifying individuals who went on to chronic psychosis (Duggan *et al*, 1989). Perhaps it was the Australian group's lack of such a continuum score that led to their failure to replicate our findings of poorer outcome among the more endogenous/psychotic depressives.

The absence of any patients in the Australian series who developed schizophrenia-like psychoses is suprising, as these have been a consistent feature of other follow-up studies of depression (Bebbington, 1982). Perhaps their cases were less severe. Alternatively, any patients who developed schizophrenia may have remained hidden among their 12 patients who refused interview or could not be traced. In our series, in which 99% of patients were traced, some of those who were most difficult to trace turned out to have chronic psychosis.

We are puzzled by the fact that our data appears to have undergone an optimistic transformation during its journey to the antipodes. We found that between 25% and 30% of patients remained always incapacitated or died by suicide; Dr Kiloh *et al* (Table IV, p. 755) report our figure as 19%. We found that one-third of our patients fell into our very poor outcome group; they report our figure as 25%. The detail of their own analysis is confusing, for they report 17% always incapacitated or dead from suicide, but then say that only 11% fell into the very poor outcome group, despite using our definition in which the former is a subset of the latter. We also wonder whether the figures in Table III (p. 754) are strictly comparable, as the Australian group describe their own as based on "proportions readmitted" rather than on survival analysis.

These differences apart, we are intrigued by the possibility that it is better to have a severe depressive illness in New South Wales than in London, particularly since the Australian endogenous patients were much older and therefore one might have expected them to fare worse. Dr Kiloh *et al* suggest that more effective treatment may be the key and point out that 10% of their whole series received lithium. We have re-examined our own casenotes and found that 20% of the London series received lithium. Perhaps we in London should recommend emigration to our patients!

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References

BEBBINGTON, P. E. (1982) The course and prognosis of affective psychoses. In *Handbook of Psychiatry*, vol. 3 (eds J. K. Wing & L. Wing). Cambridge: Cambridge University Press.

DUGGAN, C. F., LEE, A. S & MURRAY, R. M. (1989) Do different types of depression have different outcomes? *Archives of General Psychiatry* (in press).

LEE, A. S. & MURRAY, R. M. (1988) The long-term outcome of Maudsley depressives. *British Journal of Psychiatry*, **153**, 741–751.

. . . Or not?

SIR: We read with interest the papers by Lee & Murray (*Journal*, December 1988, **153**, 741–751) from London and Kiloh *et al* (*Journal*, December 1988, **153**, 752–757) from Sydney. The London paper focuses on shortcomings in previous studies on the outcome of depression and attempts to redress them. The Sydney group use a longitudinal study in a continuing attempt to validate the neurotic-endogenous classification.

A major problem with the London study is the selection of the initial cohort. We feel that the cohort is more likely to have included atypical cases. Firstly, only 17% of the subjects were from the catchment area. A significant proportion of the remainder were undoubtedly referrals for second opinion, and therefore more likely to have been atypical or severe cases. The authors attempt to counter this criticism using anecdotal evidence, but do not provide any data to rule out sample bias. The better outcome in the referred group may have been related to more aggressive treatment and follow-up. Secondly, at follow-up the sample had only four unipolar depressive patients. We are not questioning the fact that 'complications' may be an intrinsic part of depression. However, a cohort of 89 in which 3 patients have leucotomy for bulimia nervosa and 18 go on to develop other psychotic disorders is likely to have been biased towards severe or atypical cases. It would be useful to compare the rate of 'complications' between patients whose index admission was their first with those whose index admission was not their first. It would have been better to exclude patients over the age of 65 altogether, rather than include only two.

The Sydney paper makes no comment about admission patterns and possible sampling bias. Their cohort was not made up of consecutive admissions. Their follow-up was incomplete, in that of the 145 patients only 92% were traced and 72% of the survivors interviewed. Twelve refused to co-operate or could not be traced. In London more than half of the severely disabled group had lost contact with the psychiatric services. This suggests that the poor outcome group are more difficult to follow up, and may have constituted a significant proportion of the 12 who were not followed up in Sydney. In both the endogenous and the neurotic group 17% were always incapacitated by their illness or committed suicide. Yet when the London criteria were applied, only 9% and 12% in the respective groups had a very poor outcome. The poor outcome group in Sydney, therefore, appears to have been underestimated.

It is interesting to note that both groups have come up with findings that contradict their previously firmly-held but opposed beliefs about the endogenous-neurotic dichotomy. Both groups used a neurotic-endogenous classification for the cohort. When the Sydney group reclassified their cohort using DSM–III criteria they found that their sample covered the entire range of depressive illness from major depressive illness to adjustment disorder. The same spread of diagnoses may apply to the London cohort. This highlights the heterogeneity of both the samples, and casts doubts on the conclusions they make. It would, therefore, be a pity if these papers stimulated more wasteful research into the validation of the endogenous and neurotic categories.

Both studies clearly show us that a significant proportion of depressed patients do poorly in the long term. The findings of two major studies conducted in the pre-treatment era (Lundquist, 1945; Rennie, 1942) are broadly similar to those of the present studies. We wonder why it is that, almost 50 years later, with innumerable treatment methods at our disposal, we are still faced with such a dismal outcome for depression. Are we not using these therapeutic tools appropriately, or are they of no use in ameliorating the poor long-term outcome? It is unfortunate that neither of the current studies have attempted to correlate outcome with treatment. There is clearly a need for further long-term prospective studies into the outcome of depression and the effect of different treatment methods, both short and long-term, on prognosis. We hope the findings of these studies will stimulate further research into this rather neglected and difficult area.

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References

LUNDQUIST, G. (1945) Prognosis and course in manic-depressive psychosis: a follow-up study of 319 first admissions. *Acta Psychiatrica et Neurologica Scandinavica*, **Suppl. 35**, 1–96.

RENNIE, T. A. C. (1942) Prognosis in manic depressive psychoses. *American Journal of Psychiatry*, **98**, 801–814.

AIDS hypochondriasis

SIR: Todd (*Journal*, February, 1989, **154**, 253–255) describes five cases of unwarranted concerns about AIDS, "which cover a wide range of psychopathology". In several of the non-psychotic cases, there are similarities with cases of primary hypochondriasis (DSM–III–R; American Psychiatric Association, 1987), a diagnosis which has not been considered. Examination of these similarities may improve the understanding of the processes involved in such cases.

In a cognitive-behavioural formulation of primary hypochondriasis, it has been suggested that the central feature is the persistent misinterpretation of innocuous bodily sensations as indications of physical illness (Salkovskis & Warwick, 1986; Warwick & Salkovskis, 1989). As in these examples, the bodily sensations involved may be the result of a wide range of conditions, such as anxiety states, trivial physical disorders, or normal bodily variations. The resultant erroneous perception of threat to health inevitably leads to anxiety. This anxiety will be associated with a variety of other clinical features, such as avoidance, reassurance seeking, and guilt, and may resemble phobic or obsessive-compulsive states. In this view, the misinterpretation is the primary problem, and the other clinical features should be regarded as secondary phemonena, rather than "symptomatic of an underlying psychiatric disorder".

Consideration of hypochondriasis along cognitive-behavioural lines also has important implications for treatment, which are clearly illustrated by the results of Dr Todd's cases 3 and 5. Clinical experience suggests that some patients who are labelled 'poorly motivated' in fact experience high levels of anxiety, which may make them reluctant to carry out exposure treatments. It is likely that successful treatment of such cases will need to include *direct* attention to the beliefs and misinterpretations responsible for this anxiety, along with treatment directed at *secondary* symptoms. A cognitive approach may help such patients to correctly attribute their sensations and hence facilitate exposure and response prevention. Dr Todd rightly makes the point that these cases often do not respond to simple reassurance, yet case 3 "required repeated reassurance between out-patients appointments". In both hypochondriasis and obsessive-compulsive disorder it is recognised that the provision of repeated reassurance can reinforce and prolong the patient's fears (Warwick & Salkovskis, 1985). Reassurance can take the form of unnecessary physical consultations, examinations, and investigations. Once the patient's physical state has been thoroughly evaluated, none of these should be repeated without clear clinical indication. Successful treatment should teach the patient alternative methods of dealing with their concerns. Case 5 illustrates both these points successfully. The use of cognitive techniques and hyperventilation control will undoubtedly have helped this man to make more accurate interpretations of the cause of his symptoms. He sensibly refused the HIV test, for which there was no clear indication, and hence did not reinforce his anxieties.

Presentations of this type are not peculiar to AIDS. Any illness receiving publicity is likely to be associated with unnecessary concern in some individuals, other examples being syphilis or cancer. However, Dr Todd's AIDS cases serve as a timely reminder that the classification of unnecessary concerns about *all* illnesses is confused and needs clarification. It is often possible to diagnose both hypochondriasis (a somatoform disorder) and an anxiety disorder in the same case. There are no clear guidelines as to which diagnosis takes precedence, although the recent addition of an arbitary six-month duration as a criterion for DSM–III–R hypochondriasis will lead to this diagnosis being made less frequently. However, the principles of the management of the disorder should always be used where appropriate in the treatment of cases of unwarranted somatic concern.

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References

AMERICAN PSYCHIATRIC ASSOCIATION (1987) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn) (revised) (DSM–III–R). Washington, DC: APA.

SALKOVSKIS, P. M. & WARWICK, H. M. C. (1986) Morbid preoccupations, health anxiety and reassurance: a cognitive behavioural approach to hypochondriasis. *Behaviour Research and Therapy*, **24**, 597–602.

WARWICK, H. M. C. & SALKOVSKIS, P. M. (1985) Reassurance. *British Medical Journal*, **290**, 1028.

— & — Cognitive therapy of hypochondriasis. In *Cognitive Therapy in Clinical Practice* (eds J. Scott, J. M. G. Williams & A. T. Beck). Croom Helm: London. (In press).

Journal contents page

SIR: I was dismayed to find that the contents page for the Journal is no longer provided on the back cover, but inside where it is less easily glanced at. I am not aware that advertising revenue is particularly required – I believe that the Journal makes quite a lot of money for the College – and I hope the Editorial Board will revise its decision in placing the contents page inside the Journal. If it doesn't, I think it would be fair for advertisers to know that many readers will never look again at the back cover! If the purpose of the change is to facilitate binding, which certainly applies to only a small number of the published copies, perhaps a provision of a contents list for binding might be dealt with by a different means, as the needs of the general readership of the Journal are surely paramount. I hope my comments may invite some debate on this small but important unannounced matter.

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SIR: I do hope the experiment of having the list of contents on the third leaf of the Journal will end soon. Surely the front or back cover has become popular for good reason, namely ease of reference. I don't believe advertising revenue should be allowed to alter this. Perhaps, if it is unavoidable to have an advertisement on the back cover, it could be done in such a way as to allow removal of it to reveal the list of contributors.

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I am sorry that Drs Wrate and Lambert do not approve of the change to the back cover. As Dr Wrate says, the present arrangement is much more convenient for those subscribers who bind their journals. However, I agree with Dr Lambert that the new sequence of pages at the front of the issue doesn't seem to be the best possible, and a different version is now being tried. A comparison of other leading monthly journals shows a great diversity of arrangements, but most have advertising on the back cover when they can get it.

I am dismayed by Dr Wrate saying he is "not aware that advertising revenue is particularly required", in view of the enormous efforts made by the Journal staff to produce a financial surplus, which is essential to keeping the College going. I would suggest a careful look at the Annual Accounts for recent years. The alternative would be an enormous (and in the end, self-defeating) increase in subscription rates.

HUGH FREEMAN
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Obstetric liaison

SIR: The article by Appleby *et al* (*Journal*, April 1989, **154**, 510–515) was interesting to all those attempting to provide a liaison service in a general hospital with an obstetric unit. However, I was concerned that they had not received any referrals for women who had experienced miscarriages or stillbirths.

Recently I have seen two cases of women presenting as parasuicides less than a week after a miscarriage. At the time of their miscarriage they were not given any supportive counselling by nursing or medical staff, and they were expected to 'carry on as normal' after the event. This they were clearly unable to do.

I think it would be worthwhile providing training for medical staff and midwives so that they may be able to help these women in order to alleviate further psychiatric difficulties.

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Calcium techniques

SIR: Patel *et al* (*Journal*, December 1988, **154**, 849) point out additional factors for consideration in further studies of the relationship between calcium and extrapyramidal symptoms. They do not mention desirable scientific requirements of calcium assays, nor indicate whether their own collection and assay techniques involved standardisation or correction.

Firstly, the length of venostasis has a critical effect on measured serum calcium levels, for which omission of a tourniquet achieves consistency (Zilva & Pannall, 1981). Secondly, it is well recognised that ionised calcium (Ca^{2+}), rather than the total serum calcium, represents the biologically active fraction. While albumin-adjusted calcium (or corrected calcium) corresponds closely to Ca^{2+} (Larrson & Ohman, 1978), technology now permits the direct measurement of ionised calcium (Bowers *et al*, 1986).

Consideration of these factors should strengthen the interpretation of further research in this area.

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BOWERS, G. N. Jr, BRASSARD, C. & SENA, F. (1986) The measurement of ionized calcium in serum with ion-selective electrodes: a mature technology that can meet the daily service needs. *Clinical Chemistry*, **32**, 1427–1443.

LARRSON, L. & OHMAN, S. (1978) Serum ionized calcium and corrected total calcium in borderline hyperparathyroidism. *Clinical Chemistry*, **24**, 1962–1965.

ZILVA, J. & PANNALL, P. (1981) *Clinical Chemistry in Diagnosis and Treatment*, pp 455–456. London: Lloyd-Luke (Medical Books).

Neuroleptic malignant syndrome

SIR: Goldwasser *et al* (*Journal*, January 1989, **154**, 102–104) discuss the major difficulty of how to manage acute psychiatric disturbance in those concomitantly suffering from neuroleptic malignant syndrome (NMS). Their contribution to this subject is timely. However, I would like to make two points.

They state that they believe that their two cases are the first reported where definite NMS existed and terminated while the patient was still being treated with antipsychotic drugs. I reported a case in the *Journal* (McCarthy *et al*, 1988) of a similar occurrence, and these new cases represent interesting support for our conclusions in that paper.

Dr Goldwasser *et al* also discuss the value of creatinine phosphokinase measurements (CPK) in these patients. Although of definite value, there are limitations to the usefulness of these measurements. It is important to note that CPK may not be elevated at all in some cases of definite NMS (Levenson, 1985), or may only be elevated at a late stage of the illness. An elevation of CPK can also occur for many other reasons, e.g. after intramuscular injections. A measurement of CPK should therefore be only one of the criteria for the diagnosis and management of NMS.

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References

LEVENSON, J. L. (1985) Neuroleptic malignant syndrome. *American Journal of Psychiatry*, **142**, 1137–1145.

MCCARTHY, A., BOURKE, S., FAHY, J., *et al* (1988) Fatal recurrence of neuroleptic malignant syndrome. *British Journal of Psychiatry*, **152**, 558–559.

NMS and thioxanthenes

SIR: I am a little perplexed by the claim of Kemperman (*Journal*, April 1989, **154**, 562–563) that the equal D1 and D2 receptor binding characteristics of the thioxanthenes may be responsible for the low prevalence of malignant neuroleptic syndrome with this class of drugs. Although an equal binding pattern to D1 and D2 receptors has been demonstrated *in vitro*, to my knowledge the *in vivo* research using PET scan technology has shown preferential binding to D2 type receptors with only 20% to 25% D1 receptor occupancy (Farde *et al*, 1988).

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FARDE, L., WIESEL, F. A. & HALLDIN, C. (1988) Central dopamine receptor occupying in schizophrenia. *Archives of General Psychiatry*, **45**, 71–78.

Schizophrenia, season of birth, and maternal age

SIR: Dalen (*Journal*, December 1988, **153**, 727–733) demonstrates, with British and Swedish data, increased seasonal variation of births associated with raised maternal age. He thus provides a possible explanation for the season of birth effect in schizophrenia, given the previous observations that maternal age at birth is raised in samples of schizophrenic patients. In addition, he suggests that the observed excess of births by older women in the early months of the year is due to age-related decline in their fertility. The essence of this argument is that a cohort of such women will be older, and hence less fertile, in the later part as compared to the earlier part of the year. Although true, this is concerned with a cohort, not an age class, and is therefore not directly relevant. His example of a cohort of women born in 1935, who will be in the age class 15–19 from 1951 to 1954, demonstrates an apparent seasonal effect only because the time interval considered begins at the beginning of one year and ends at the end of another year. However, the arbitrary convention that January is the first month of the year is irrelevant to age calculations, and more appropriate time intervals to consider would be those which begin on the 15th birthdays and end on the 20th birthdays of the cohort. These time intervals are precisely when the cohort will be in the age class 15 to 19, but can begin and end at any time of the year. When a time interval begins at the beginning of one year, and ends at the end of another year, then the rising fertility in this age-range results in an excess of births in the later months of the year. However, when a time interval begins in the middle of one year, and ends in the middle of another year, the rising fertility produces the opposite effect – an excess of births in the earlier months of the year. Considering the entire cohort, there will not be an obvious overall seasonal effect.

The increased seasonality of birth associated with raised maternal age is probably related to the decline in fertility in a different way. Consider fertility to be composed of two additive components: the first representing the level of fertility, which is relatively stable but changes with age; and the second representing the superimposed fluctuations which occur regularly at one cycle per year. The ratio of the amplitude of the seasonal fluctuations to the level of fertility will then be a determinant of the apparent magnitude of the seasonal variations of births. It is possible that this ratio increases as fertility level falls with advancing age, and results in the increased seasonal variation of births in the older age groups as demonstrated by Dr Dalen. This explanation does not have the difficulty raised by Dr Dalen with his argument that southern hemisphere studies of schizophrenia show an excess of births which is not at the beginning of the year.

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Homosexual erotomania

SIR: We were interested to read Dunlop's account (*Journal*, December 1988, **153**, 830–833) of two cases of female homosexual erotomania. This has been reported before (Lovett Doust & Christie, 1978; Signer & Cummings, 1987).

Dr Dunlop equates erotomania with de Clérambault's syndrome, but we feel that her cases do not meet the criteria for de Clérambault's syndrome. De Clérambault formulated the 'fundamental postulate' which describes the essential characteristics of the condition: the conviction within the patient (the subject) of being in amorous communication with a person of higher social status (the object), who has been the first to fall in love and the first to make advances (Enoch & Trethowan, 1979). Neither of Dr Dunlop's cases appear to hold the delusional belief that the other person (in both cases another woman) is in love with her. Her first patient's love object "approached her first, expressing concern and wishing to be helpful". There is no evidence that the patient believed the object to have had any amorous interest in her. Her second patient experienced the abrupt onset of "something special" between herself and the object and developed an obsessional attachment to her. She hinted at "more than platonic" feelings for the object, but no mention is made of belief in reciprocation by the object.

In Dr Dunlop's Table I she omits Ellis & Mellsop's (1985) criterion (C): "The other person had been the first to fall in love". Had this been applied, it would perhaps have been made clear that neither patient believed the object to be in love with her.

This diagnostic confusion stems from ambiguous usage of the term 'erotomania' to include a wide variety of types of pathological attachment behaviour. It is sometimes taken to indicate delusional love by the patient for another person, although in the de Clérambault syndrome the belief is of a love which is in precisely the opposite direction, i.e. from the object to the subject.

Enoch & Trethowan (1979) remarked on the importance of distinguishing erotomania from everyday infatuation, normal passion, and nymphomania on the one hand, and paranoid schizophrenia on the other, but in the absence of clear definitions it becomes impossible to make these distinctions. Seeman (1978) pointed out that there is much overlap in the literature as to what is meant by the terms phantom lover syndrome, erotomania, and de Clérambault's syndrome. The resulting uncertainty is amply demonstrated in Ellis & Mellsop's (1985) review of 58 cases, supposedly of de Clérambault's syndrome, of which only 11 (19%) fulfilled the 'fundamental postulate' criteria (A, B, C, and D) which they adopted.

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ELLIS, P. & MELLSOP, G. (1985) De Clérambault's syndrome – a nosological entity? *British Journal of Psychiatry*, **146**, 90–95.

ENOCH, M. D. & TRETHOWAN, W. H. (1979) *Uncommon Psychiatric Syndromes* (2nd edn). Bristol: John Wright.

LOVETT DOUST, J. W. & CHRISTIE, H. (1978) The pathology of love; some clinical variants of de Clérambault's syndrome. *Social Science and Medicine*, **12**, 99–106.

SEEMAN, M. V. (1978) Delusional loving. *Archives of General Psychiatry*, **35**, 1265–1267.

SIGNER, S. F. & CUMMINGS, J. L. (1987) De Clérambault's syndrome in organic affective disorder. *British Journal of Psychiatry*, **151**, 404–407.

Post-traumatic stress disorder

SIR: McFarlane's account of a bushfire (*Journal*, February 1989, **154**, 221–228), while elegant in its methodology, is perhaps not capable of generalisation to post-traumatic stress disorder (PTSD) as a whole. He points out that most of the recent literature focuses on Vietnam veterans and victims of disaster. These groups, however, differ significantly from Dr McFarlane's. Vietnam veterans were an unmotivated, socially disadvantaged group of draftees who were hardly prepared for what they faced, and victims of a disaster are a more heterogeneous group and are, by definition, completely unprepared for the trauma they experience. Dr McFarlane describes his group as large, trained and volunteer. They were recruited into the traumatic event after it started, were well motivated, and possibly had previous experience. It thus, by definition, lacked the element of surprise and unfamiliarity experienced by the other PTSD groups examined.

It may well be that this element of unpreparedness would account for the development of PTSD in some sufferers.

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Neuronal misconceptions

SIR: Goodman (*Journal*, March 1989, **154**, 292–299) has set himself the difficult task of suggesting that anomalous neural connections underlie some psychiatric disorders. He has commendably suggested tests for his hypothesis. Nevertheless, it suffers from inherent difficulties. Firstly, it incorporates a two-stage pathogenesis: a primary lesion (e.g. brain damage) followed by maladaptive neuronal repair. The dual abnormalities would be more difficult to test in the clinical setting than more simplistic explanations, such as 'neuro excess' theories. Secondly, his attempts to explain a range of psychiatric abnormalities on the basis of misconnections have forced him to make simplistic generalisations, e.g. the dichotomisation between focal and diffuse misconnections, and their likely consequences. If, as he implies, abnormal (and by inference, *random*) misconnections lead to behavioural abnormalities, it is unlikely that such abnormalities take the form of consistent syndromes. Finally, a misconnection theory need not exclude other hypotheses. Indeed, 'misconnections' could lead to 'neuroexcess' or 'neurodeficiency'.

The relationship between temporal lobe epilepsy (TLE) and schizophrenia illustrates the difficulty of proving or disproving hypotheses of the sort proposed by Dr Goodman. While TLE has been associated with a number of psychiatric states (Vasquez, 1952), its link with schizophrenia has been debated (Small *et al*, 1986). Dr Goodman focuses on the increased prevalence of schizophrenia among patients with TLE due to alien tissue lesions, but neglects other factors which appeared to play an equally prominent role in Taylor's series, viz., sinistrality and femininity (Taylor, 1975). While the discrepancies in prevalence of schizophrenia between alien tissue lesions and mesial temporal sclerotic lesions may be attributed to differences in the likelihood of misconnections following these two lesions, other explanations cannot be ignored. These include differences in the topography of the two types of lesions. Moreover, temporal lobe alien tissue lesions may be accompanied by similar lesions in other brain regions. The latter could account for the psychopathology. A more provocative explanation for the alien tissue/mesial sclerosis discrepancy – that mesial sclerosis arising from perinatal lesions *protects* against schizophrenia – may not be acceptable to proponents of the aetiological role of obstetric trauma in schizophrenia (Murray *et al*, 1988).

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References

Murray, R. M., Lewis, S. W. & Reveley, A. M. (1985) Towards an aetiological classification of schizophrenia. *Lancet, i*, 1023–1026.

Small, J. G., Small, I. F. & Hoyden, M. P. (1966) Further psychiatric investigations of patients with temporal and non-temporal lobe epilepsy. *American Journal of Psychiatry*, **123**, 303–310.

Taylor, D. C. (1975) Factors influencing the occurence of schizophrenia-like psychosis in patients with temporol lobe epilepsy. *Psychological Medicine*, **5**, 249–254.

Vasquez, J. (1952) Epilepsies temporales et manifestations mentales. *Union Medicale du Canada*, **81**, 1062–1068.

Unreliable urine samples

Sir: I was very interested to read the results of Gossop *et al's* follow-up of opiate addicts after treatment (*Journal*, March 1989, **154**, 348–353). I am, however, a little unhappy about their use of urine specimens to support claims of abstinence, as in my experience such testing is not sufficiently reliable for such inferences to be drawn. It is difficult, without undue strain to the doctor-patient relationship, to be sure of the origins of a proffered sample. I feel that urine drug screening is often a test of uncertain accuracy, performed on a sample of dubious antecedents, provided by a population noted for the deviousness of their behaviour. It has a place in the assessment of drug use, but added little to Dr Gossop *et al's* study.

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Munchausen's syndrome by proxy

Sir: Munchausen's syndrome by proxy has been called the "hinterland of child abuse" (Meadow, 1977) and there have been numerous, and sometimes quite bizarre, case descriptions. The parents are known, by using fabrication and manipulation, to cause their children to receive unnecessary and potentially harmful investigations and treatment. The presenting problems can vary widely and include neurological symptoms, haematuria and bacteriuria, recurrent diarrhoea and bloody stools, vomiting, dehydration, drowsiness, and urticaria. The management of this disorder can present quite a challenge to health professionals (Nicol & Eccles, 1985; Rosen *et al*, 1983). I report a case with an unusual presentation of self-induced vomiting, anorexia, and weight loss in a 3-year-old girl.

Case report: A 3-year-old girl was admitted to the paediatric ward via her general practitioner, after having been ill for 5 days with an upper respiratory tract infection and perhaps a mild chest infection, for which she had been treated with amoxycillin. This would not in itself have merited admission, but the girl's mother complained that the girl was refusing to eat or drink, and was making herself vomit by "sticking her finger down her throat", hence becoming dehydrated. The girl had been admitted to a hospital in Leeds nine months before this admission and had presented with "vomiting and food refusal". Her mother was very concerned about the child's condition, and repeatedly asked the doctors to set up a drip as she felt her child was "very dehydrated".

Child psychiatric opinion was sought, and it soon became clear that the child's mother was suffering from bulimia nervosa. She gave clear descriptions of bingeing and self-induced vomiting since she was a teenager. Her life had been unsettled and her relationships short-lived. Her child's father left before the child was born, and the mother then lived with another man with whom she had another child. He also left, after much conflict at home, and took their two-year-old girl with him. Now the mother is seeing another man and is pregnant again.

She described her own childhood as "terrible", as her own mother died from "not eating" and she and her sister were brought up from an early age by her maternal grandmother, who was very strict and would beat the children "until they stopped crying". The mother left home as soon as she could and tried to pass examinations in nursing but was unsuccessful. She worked as an auxiliary nurse before having her first baby. She has had numerous admissions into various hospitals for short spells with "non-specific" problems, leaving the child in voluntary care or with friends. Her last admission was for suspected ectopic pregnancy after she collapsed on the paediatric ward while visiting her daughter, who had been readmitted with self-induced vomiting. The mother was discharged after a short period of observation.

We encouraged the mother to attend for individual psychotherapy, with a view to helping her cope with her chaotic life and improve the relationship with her daughter.

In Munchausen's syndrome by proxy the children do not have a good prognosis, especially if the parents themselves suffer from Munchausen's syndrome. Markantonakis & Lee (1988) suggested a central register of Munchausen's syndrome patients which could prove to be a cost-saving exercise (Jones, 1988). I would like to suggest the same for Munchausen's syndrome by proxy, as this may be a way of alerting clinicians in different parts of the country which would lead to early recognition of the problem.

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JONES, J. R. (1988) Psychiatric Munchausen's syndrome: a College register. *British Journal of Psychiatry*, **153**, 403.

MARKANTONAKIS, A. & LEE, A. S. (1988) Psychiatric Munchausen's syndrome: a College register. *British Journal of Psychiatry*, **152**, 867.

MEADOW, R. (1977) Munchausen syndrome by proxy. The hinterland of child abuse. *Lancet*, *ii*, 343–345.

NICOL, A. R. & ECCLES, M. (1985) Psychotherapy for Munchausen syndrome by proxy. *Archives of Disease in Childhood*, **60**, 344–348.

ROSEN, C. L., FROST, JR, J. D., BRICKER, T., *et al* (1983) Two siblings with cardiorespiratory arrest: Munchausen syndrome by proxy or child abuse? *Paediatrics*, **71**, 715–720.

Sorcery and psychiatry

SIR: Keshevan *et al* (*Journal*, February 1989, **154**, 218–220) describe how psychiatric illness is attributed to sorcery in the predominantly Hindu culture of southern India.

In our child psychiatry practice among Moslem Bangladeshi clients we found a similar pattern. A wide variety of physical and emotional disorders are thought to be caused by sorcery. This can be of two types: *Kunni*, when someone who envies their victim casts a spell; and *Ufri*, when a chance circumstance caused by somebody leaving the house causes possession. Bhattacharyya (1986) describes a similar pattern in Hindu Bengal. In Bangladesh, clients consult a local religious healer, a Mullah, as well as practitioners of western medicine. He may use hair or leaves to create an alternative spell to counteract the initial spell or possession. Alternatively, he may treat the patient with an amulet containing verses from the Koran to be worn round the neck or arm, or give the patient holy water or holy mustard oil over which Koranic verses may have been read or into which paper with Koranic verses on may have been dipped.

The commonest symptoms which we found described to sorcery are conversion disorders or psychosomatic symptoms.

Case report: An 11-year-old Bangladeshi girl who had spent all her life in England had been given an injection at the age of 5, and following this the family described a personality change in which she became much more shy. The Mullah suggested she had been possessed, and she had been given holy water to drink. She was diagnosed as having epilepsy at the age of 9 and had both grand and petit mal fits which were controlled with sodium valproate.

Her sister had died in Bangladesh at the age of 11 after a 2-year illness characterised by odd behaviour. The father's side of the family accused her mother and uncle of casting a spell on her, but the mother thought that the illness had been caused by her standing under a tree at an inauspicious time.

The patient was a shy girl who had been teased about her fits at primary school. A few weeks after starting secondary schooling at a large comprehensive school she had a "florid fit" and did not return to school that term. The paediatrician thought that her frequent fits were hysterical, and referred her to a psychiatrist.

She was having attacks in which for no apparent reason she would look scared and thrash around. Sometimes she would attack the younger children in the house, trying to strangle them or try to pick up a knife, or at other times she would try to bite people. When she came out of the 'fits' she would cry a lot and say she "hurt everywhere". Her mother thought that she had been possessed by going outside alone during the school lunch hour and sitting on the grass. They were concerned that she would die like her older sister. They had consulted a Mullah, who had given her holy water to drink.

In addition to the stress of starting a new school, she was missing her father. He had gone to Bangladesh just prior to the onset of these attacks. He was staying with his mother who was dying and had no plans to return to England. The family had housing problems and their son was in trouble with the police.

The family were reassured both by the paediatrician and by the psychiatrist that the fits were not epileptic. They knew that the fits were precipitated by situations where she felt stressed. For example, one of the attacks had occurred when she was talking about her sadness in her father's absence. The family followed the psychiatrist's advice and ignored the attacks. The attacks ceased when they were positively connoted as her way of trying to solve family problems in the absence of the head of the household and to provide a reason for him to return to England. She was slowly reintroduced to her school and had no fits there.

This family accepted the concepts of western medicine: they attended appointments punctiliously, followed the tasks set by the psychiatrists, and gave the patient her medication regularly. Her mother, however, also told us that the Mullah had told her that her daughter had been possessed since she was 5 and that the possession had now got into her blood. Her mother therefore intended to give her holy water until she was totally well. One sign of her possession was the fact that she did not like learning the Koran and did not like having it read to her.

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Solvent abuse psychosis

SIR: Although much has been written about the consequences of solvent abuse, including associations with cerebral atrophy and cerebellar degeneration (Fornazzari *et al*, 1983), no discrete psychiatric syndromes have been associated with this habit. Claims of schizophreniform psychosis have been made (Alapin, 1973; Lewis *et al*, 1981), but these have been regarded as anecdotal (Ron, 1986). An increasing number of chronic solvent abusers are being seen in our hospital, all of them being native Canadians, and a pattern of psychiatric morbidity is emerging. We outline the details of one such case, and suggest that there is a specific psychiatric state which results from chronic inhalation of toluene-containing adhesive mixtures

Case report: Mr R, a twenty-year-old man, was brought to our hospital by the local police, having been found wandering on the highway near his home. At interview, he was noted to have adhesive on his face and his breath was tinged with acetone. Mental state examination revealed a considerable degree of disorientation and his thought content had marked paranoid features. Mr R admitted to hearing condemnatory voices, and he experienced religious-type visual hallucinations on occasion. A toxic confusional state was diagnosed and antipsychotic therapy was started.

Four weeks later, Mr R continues to display a fluctuating level of consciousness, and both auditory and visual hallucinations persist. He continues to have paranoid ideas about the staff, and displays marked irritability. There is no previous history of paranoia, and no family history of schizophrenia. Mr R has inhaled adhesive solvents for more than 7 years, and has done so at least five times per week on average.

This patient has a persistent paranoid psychosis with features of a toxic confusional state. We attribute this problem to a lengthy history of solvent abuse, and his symptoms have failed to respond to conventional antipsychotic medications. He is only one of a number of such patients in our hospital. Having compiled a series of them, certain definite features are emerging. Our findings suggest that prolonged solvent abuse can cause a protracted paranoid psychosis which is extremely slow to resolve. Our plan is to follow our series of patients to test the validity of the hypothesis that such paranoid states are directly attributable to solvent abuse.

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ALAPIN, B. (1973) Trichloethylene addiction and its effects. *British Journal of Addiction*, **68**, 331–335.

FORNAZZARI, L., WILKINSON, D. A., KAPUR, G. M., et al (1983) Cerebellar, cortical and functional impairment in toluene abusers. *Acta Neurologica Scandinavica*, **67**, 319–329.

LEWIS, J. D., MORITZ, D. & MILLIS, L. P. (1981) Long-term toluene abuse. *American Journal of Psychiatry*, **138**, 368–370.

RON, M. A. (1986) Volatile substance abuse: a review of possible long-term neurological, intellectual and psychiatric sequelae. *British Journal of Psychiatry*, **148**, 235–246.

A HUNDRED YEARS AGO

Society for the study of inebriety

A general quarterly meeting was held in the rooms of the Medical Society last Tuesday, the President, Dr Norman Kerr, in the chair.

A paper on Inebriety among the Cultured and Educated Classes was read by Dr James Stewart, of Dunmurry, Sneyd-park, Clifton, who gave a *résumé* of observations based on twelve years' experience in the treatment of inebriates. Dr Stewart called special attention to the pathological condition of the cerebral tissue in inebriety, a loss of brain substance as real as the loss of a portion of a finger sliced off accidentally with a knife. Inebriety was a physical disease as clearly marked as many other diseases, and must, to be successfully treated, be dealt with in as scientific a manner as these other maladies. New and sound brain tissue must be built up before a cure could be effected. This required a considerable time, the shortest term being twelve months. Dr Stewart concluded by stating as his opinion that (1) inebriety is a lesion of the brain which has gone so far as to affect the will power; (2) successful treatment based on this pathological dictum must include the absolute cessation of alcoholic drinking: (3) there is no danger in the sudden and complete withdrawal of alcohol if the case, no matter how severe, be in the hands of a skilful physician able to personally direct the hourly treatment from the first; (4) the physician undertaking the charge of such cases ought to be himself a total abstainer, so that moral treatment by example might supplement therapeutic remedies; (5) permanent recovery need not be hoped for unless both lines of treatment be pursued systematically during an uninterrupted period of twelve months in a "home" from which alcohol is entirely excluded; (6) so-called cures effected by bark, strychnine, iron, and other specifics have not proved permanent; (7) the permanence of a cure depends greatly on the after-treatment pursued subsequently to the patient leaving the "home". The family of the inebriate should all become total abstainers, no alcohol being allowed under any circumstances into his or her house except as a drug prescribed by a medical man, and dispensed in a medicine bottle.

Reference

The Lancet, 5 January 1889, 26.

Researched by Henry Rollin, Emeritus Consultant Psychiatrist, Horton Hospital, Surrey

British Journal of Psychiatry (1989), **155**, 134–138

Books Reconsidered

The Doctor, His Patient and the Illness: Michael Balint*

Remembering where you were when Jack Kennedy died has become a favourite question to ask of people of an age to remember that day in November 1963. For a certain generation of general practitioners, a not dissimilar question might be, "When did you first read *The Doctor, His Patient and the Illness?*" Balint's impact on general practice is remarkable and unquestioned. His book, first published in 1957, appears among the top ten, if not the top three, that all new entrants into general practice 'must read'. Yet the paradox is that few, if any, trainees will actually read his book, that Balint groups have a falling membership, that the Balint Society, founded after his death by a group of GPs, is on the periphery of modern general practice thinking, and that few if any permanent developments have come from his followers. Balint might well be excused if he paraphrased the quote attributed to Jung, "Thank God I'm Balint and not a Balintian".

The context

To appreciate Balint's work on general practice, it is important to set it in the context not only of the state of general practice and of psychoanalysis, but of much of Balint's own background and training. He was born in Budapest in 1896. His father was a GP, an often forgotten fact, and after completion of his own medical studies Balint trained in the Hungarian Institute of Psychoanalysis and was analysed by Ferenczi. The Hungarian system of psychoanalytic training differed in one essential form from the practice traditionally adopted in Vienna and Berlin: the supervision of the candidate's first case, or cases, was carried out by the candidate's training analyst. Balint writes in the section on training, "In the Hungarian system the interrelation of the transference of the patient and the counter-transference of his analyst is in the focus of attention right from the start and remains there. In the Berlin system the counter-transference of the candidate to his patient is by tacit agreement not dealt with in supervision but is left to be worked through in his personal analysis". Balint brought his experience of the Hungarian system to England and experimented with it in part in the groups he developed for GPs.

Like many of his European colleagues, Balint left Europe just before the war and eventually settled in London, where he quickly obtained a consultant post both at University College Hospital and at the Tavistock Clinic. This was in the early 1950s; the National Health Service had been launched, and the separation of general practice from specialised medicine had become organised and institutionalised. General practice as a separate discipline did not exist in any fundamental form and, for many medical students, entering general practice was seen as a failure. They had fallen off the ladder: the Royal College of General Practitioners did not yet exist, and the medical establishment, in the form of Lord Moran, was actively derogatory of general practice. When the possibility of a separate College of General Practitioners was suggested, his famous remark, "Over my dead body", still rankles with many of the active GPs of that time. General practice had to wait till the early 1960s for its renaissance. The work of Michael Balint, and the publication of the book in 1957, were critical points in the emergence of this new discipline.

Psychoanalysis in the late 1940s and 1950s had itself emerged as a clinical entity in its own right, and the Tavistock Clinic had quickly become a centre of national and international excellence. The scientific basis to this new form of treatment was, and still is, disputed, but it had gained a place within the public service sector, and under the leadership of Sutherland, psychoanalysts at the Tavistock were encouraged to explore how the theoretical insights derived from their work might be applied to individuals, groups and institutions not directly involved in the practice of psychoanalysis. It is against this background that Balint, together with his wife Enid, started the research project at the Tavistock Clinic that was to lay the foundation for *The Doctor, His Patient and the Illness*.

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*London: Pitman (1957).

The work and the ideas

Michael and Enid Balint had already begun to apply that psychoanalytic experience to the training of social workers involved in marital work. In 1954 they 'collected' a group of GPs to take part in research seminars. Initially this focused on the drugs usually prescribed by GPs. Balint soon realised that the most frequently prescribed drug was the doctor himself, and the seminars evolved into an exploration of "the doctor as a drug". Weekly meetings followed over a number of years, and transcripts were kept of the seminars. Doctors presented cases they encountered in their daily work, and together with the Balints explored and analysed their patterns of work. As the seminars progressed it was possible to identify recurring problems, and Balint, in the introduction to the first edition of the book, defines it thus: "Why does it happen so often that in spite of earnest efforts on both sides, the relationship between patient and doctor is unsatisfactory and unhappy? What are the causes of this undesirable development and how can it be avoided?" The chapter headings of the book are in part the responses to this particular question. Phrases such as "the apostolic function", "collusion of anonimity", "underlying diagnosis", "ticket to the door", "dilution of responsibility", and "teacher-pupil relationship" are all examples of the immense creativity present in those original research seminars. These phrases have a simplicity and depth which ensures their immortality.

However, it was not long before the flaws began to appear. Balint's enthusiasm for the 'psychological' took over and he could not avoid encouraging the participants to develop their psychotherapeutic skills. Understandably, the model offered was psychoanalytic and psychodynamic. Many GPs began seeing patients for one hour after a busy surgery, and rather than learning from the seminars about the limitations of the psychoanalytic model, they experienced all the problems of the untrained psychotherapist. Many had learnt how to start, but few had understood the importance of when to stop, or indeed, how to stop. Thus the caricature of the Balint-trained doctor as a Detective Inspector ferreting around for the culprit cause also became part of the mythology of Balint groups and is unfortunately still present today.

Balint failed to give due emphasis to physical factors in psychotherapy as well as psychoanalysis. His closest consideration of the body was when he underlined the importance of non-verbal behaviour. He rightly challenged the "elimination of the cause by appropriate physical examination", but in so doing encouraged the mind-body split which plagues both the practice of psychoanalysis and organic medicine. Balint focused on the psychological aspects of general practice and helped to raise the doctors' awareness of the factors involved in the complex interactions occurring in their consulting rooms. As long as he remained in the role of 'anthropologist' his contributions were, and are, of immense value. When he crossed the boundary and became a clinician and teacher, his interventions began to have an impact which he at times denied and at times decried. Several of the original group of Balint-trained doctors left general practice and took up psychotherapy or psychoanalysis full-time. Even though he saw this development as a failure of the group work, it became very difficult to stop the trend. For the next few years, Balint experimented with the notion of focal and brief psychotherapy, and it seemed that he was developing a model of psychotherapy more suited to the needs of general practice. However, it became clear through the work of Malan and others that it required even greater skill and experience to make the appropriate assessment necessary for short-term work. In any case, what was described as short-term work involved 30–40 one-hour sessions, a totally impractical option for GPs to consider seriously. Nevertheless, when Balint died in 1970, his impact on general practice was assured and the work he initiated was continued by a small but loyal group of disciples.

Balint's essential contribution to general practice was to use his psychoanalytic training and knowledge to describe, explore, and illuminate the nature of general practice. Instead of the "doctor as a drug" or the "doctor's feelings", read counter-transference. Instead of the "presenting symptom as the ticket to see the doctor", read "unconscious motivation". He reminded doctors trained in the medical model that psychological problems can often present as physical symptoms – not a new concept, but one that freed many practitioners from the limitations of their medical education. Balint challenged the notion of the objective scientific doctor standing or sitting at a distance from his patient. He demonstrated how not only treatment but the diagnosis is formed as a result of an interaction between doctor and patient. And finally, he provided a model for training doctors to develop their psychological skills within their consulting rooms. Like all pioneers, he overstated his case, but the caveats, doubts, and cautionary comments which are to be found in his writings have only partially been explored by the majority of his followers.

Following the work Balint did on brief psychotherapy, he undertook a research study on the use of repeat prescriptions in general practice. The results of this work were published after his death in a book entitled *Treatment or Diagnosis* (Balint, 1970). Further books published by his colleagues – *Patient Centered Medicine* (Hopkins, 1972), *Six Minutes for the Patient* (Balint & Norell, 1973), *The Human Face of Medicine* (Hopkins, 1979), and *While I'm here Doctor* (Elder & Samuel, 1987) – have attempted to develop the work undertaken by Balint in the 1950s. While the thrust of Balint's descriptive analyses of general practice consultations still stands the test of time, there has been a recognition that the caricature of the Balint-trained doctor as a 'Detective-Inspector' is all too often an accurate description. Balint's concept of the "the doctor as a drug" and the role of the doctors' emotions were probably his greatest gifts to general practice. However, there is a clear danger of confusing emotional curiosity with caring, and much of the criticism levelled at Balint stems from this misunderstanding. The more recent work described in the later work by his colleagues focuses on freeing the doctor from discovering *why* so that he can observe *how* the patient talks, thinks, feels, and behaves the way he does. The patient is given permission to complain about anything, and the doctor has to learn to bear the frustration, uncertainty, and helplessness that are inherent characteristics of the human condition. This is a far cry from the 'long hour' and the 'focal therapy' with the notion of 'selective attention' and 'selective neglect' that were the hallmarks of Balint's work in the 1950s and 1960s.

Balint seminars

The second major outcome of Balint's work, which is also well-described in his original book, was the method of training. Balint recognised that to suggest that all doctors, let alone health-care workers, should have a personal analysis was not only totally impractical but also likely to be laughed at. Nevertheless, he realised that for GPs to work at a psychological level with their patients required "a limited though considerable change in the doctor's personality". This statement, like the concept of "the doctor as a drug", remains as a testament to Balint's courage and genius. Psychoanalysis had for many years recognised the importance of a personal analysis as part of the training necessary for a therapist. Balint attempted to borrow from psychoanalysis and adapt to the needs of general practice. The structure of the seminars involved a group of doctors meeting weekly where cases were presented. As Balint himself wrote: "Our chief aim was a reasonably thorough examination of the ever-changing doctor-patient relationship, i.e. the study of the pharmacology of the drug "doctor". Balint discouraged any preparation or formal case-presentation, and through his interventions would facilitate a frank account of the emotional aspect of the doctor-patient relationship. "The doctors tried hard to entice the psychiatrists into a teacher-pupil relationship but for many reasons it was thought advisable to resist this. What we aimed at was a free give-and-take atmosphere in which everyone could bring up his problems in the hope of getting some light on them from the experience of others".

In the second half of *The Doctor, His Patient and the Illness* Balint describes this method of training, and in a further book, *A Study of Doctors* (Balint, 1966), he provides the evaluation of results in much greater detail. Balint groups have continued since their development in the late 1950s. However, outside the Tavistock Clinic they have not taken root with any great success and attempts to introduce similar methods of training for medical students and general practice trainees have largely been unsuccessful. Part of the reason for this is that the leaders of Balint groups may not be explicit about their objectives. Thus members often attend with different expectations from those of the leaders and are put on the defensive: this is especially so if the leaders' expectations are kept covert. Whatever the leaders' or members' expectations may be, during the course of such groups both soon recognise that the boundary between personal issues and professional concerns is difficult to maintain. As doctors reveal information concerning their approach to their patients, they inevitably reveal and face their own values, prejudices, and belief systems. This may lead to an uncomfortable realisation that the defence systems they choose to adopt in their professional lives are similar to those in their personal lives. For some, this is a new and public discovery that is nevertheless welcomed. For others it can come as an unwelcome and painfu shock. Balint was aware of this problem from the outset, but was determinedly against the groups developing into therapy sessions. He attempted to select and screen out those doctors who were seeking therapy and discouraged personal revelations in the group. He did not think that the group should be a substitute for therapy, yet one of Balint's origina ideas was to copy the Hungarian psychoanalytic training model. In this method the analysand receives both analysis and supervision of his first case by his analyst – i.e. the supervisory (training) and therapeutic (treatment) roles are combined. The analysand is thus able to discuss his own feelings towards his patient (counter-transference) with an analys who is familiar with the analysand's interpersona and intrapsychic problems. Balint's aim was "to help doctors to become more sensitive to what is going on consciously or unconsciously in the patient's mind when doctor and patient are together". Yet in the seminars, Balint limited himself to commenting only on the doctors' *public* and *conscious* statements. He did not comment on or interpret any covert or unconscious material that he observed. Any statements involving personal problems were actively discouraged and not taken up. In addition, Balint, although recognising the importance of the doctor/group leader relationship and the doctor/rest of the group relationship, tried to avoid discussions of an interpersonal and intimate nature that involved these areas.

Bacal (1972) suggested that Balint training primarily affects what he has termed the 'area of professional ego'. He suggested that change in this area is "related to the capacity of a doctor to free up and convert enough of his pre-occupation and anxiety over personal problems into what we call the therapeutic interest or curiosity, so that he is in a position to do a good professional job". Bacal went on to infer that although Balint was aware of the need to mix the training and treatment models, he did not utilise the Hungarian system to its full extent. Bacal describes the case of a young doctor who, after attending Balint seminars for three years, still experienced considerable inhibitions with his younger women patients. He attended psychotherapy for eight months and subsequently reported much improvement in his ability to work with such patients. The issue Bacal raised was whether a doctor could have derived the help he obtained from psychotherapy while attending a Balint group. To be fair to Balint, he was aware of the potential limitations of his method of training: "I am aware that by all this I have not said much about these self-imposed limitations of our interpretations, and furthermore that by this simplified description I have deliberately disregarded a number of dynamic complications. Lastly, whether or not these limitations can be adhered to in the long run, or how necessary or desirable it is to adhere to them, is another matter, and only further experience can decide". It is a sad reflection on the work of the Balint Society that few, if any, such experiments have been encouraged. The developments in general practice education in this area have largely come from other workers (Lurie & Gallagher, 1972; Marinker, 1972; Heron, 1973; Freeling, 1982; Pietroni, 1984).

The critics

It is unfortunate that Balint's critics in general practice have limited themselves to his original book. Balint's psychoanalytic writings are largely ignored, and the serious attempts he made to evaluate the outcome of the training method are difficult to obtain. The criticisms have centred around the scientific/unscientific nature of psychoanalytic theories and the limited understanding Balint had of the nature and task of general practice. Sowerby (1977) provided the most cogent attack on Balint, which can be summarised as follows:

(a) Balint made the irrefutable conjecture (unscientific) that a scientific understanding of human behaviour was possible in theoretical terms, and believed that general practice is primarily concerned with psychological problems.
(b) He believed that psychological illness should not be diagnosed by exclusion, and that the diagnostic process was one of description rather than identification.
(c) He initiated a confusion of language and proliferation of jargon which privileges the verbally articulate and the emotionally demonstrative.

Sowerby's paper has itself been rightly criticised, but his views represent a major section of general practice thought and practice. It is ironical that those that disagree with Sowerby will also find Balint's ideas and training methods limited, but for very different reasons. Balint failed to give due emphasis to physical factors in psychotherapy or psychoanalysis. Ignoring the body and its effect on the mind is a fundamental omission of psychoanalytic theory, just as the omission of the mind and its importance to the body has plagued 'scientific' medicine.

Balint had an enquiring and original mind. He experimented with different techniques, but largely stayed within the accepted psychoanalytic framework. This has had a stultifying influence on psychotherapeutic approaches in general practice. Behavioural approaches, the use of transactional analysis, co-counselling, and humanistic models of group psychotherapy have not had sufficient use or impact because the individually-based psychodynamic and psychoanalytic model, as practised by Balint, has been so influential within general practice. In addition, the educative nature of the task of general practice has been overly influenced by Balint's misunderstood views of the 'apostolic' function of the GP. Balint wrote: "It was almost as if every doctor had revealed knowledge of what was right and what was wrong for patients to expect and to endure and further as if he had a sacred duty to convert to his faith all the ignorant and unbelieving among his patients". It seemed that Balint was challenging the assumption that doctors should advise, reassure, direct, influence, and suggest. Under the influence of Balint training, many GPs learnt "how to listen" in a particular way and how to become less intrusive and 'non-directive'. The idea that the 'non-directive' approach is non-directive is, of course, nonsense. Balint's views on this issue were also quite clear: "It does not matter whatsoever whether the doctor shuts his eyes and refuses to see what he is doing or accepts his role and chooses consciously what he teaches – teach he must".

Balint *was* a great teacher, although characteristically he declined to accept his undoubted charisma and influences. The mark of a truly creative and civilised mind is that it can hold paradoxically opposing viewpoints on an issue at one and the same time. Judged by this criteria, Balint showed marks of genius, and we all owe a great debt to his father, a general practitioner!

References

Bacal, H. A. (1972) Balint groups: training or treatment. *Psychiatry in Medicine*, 3, 373–377.

Balint, M. (ed.) (1966) *A Study of Doctors*. London: Tavistock.

— (1970) *Treatment or Diagnosis*. London: Tavistock.

Balint, E. & Norell, J. (1973) *Six Minutes for the Patient*. London: Tavistock.

Elder, A. & Samuel, O. (1987) *While I'm here Doctor*. London: Tavistock.

Freeling, P. (1982) *In-Service Training – A Study of the Nuffield Courses of RCGP*. Windsor: NFER/Nelson.

Heron, J. (1973) *Course for New Teachers in General Practice*. Human Potential Research Project. Guildford: University of Surrey.

Hopkins, P. (ed.) (1972) *Patient Centered Medicine*. London: RDP Ltd.

— (ed.) (1979) *The Human Face of Medicine*. London: Pitman Medical.

Lurie, M. J. & Gallagher, J. M. (1972) Innovative techniques for teaching psychiatric principles to general practitioners. *Journal of the American Medical Association*, **221**, 696–699.

Marinker, M. (1972) A teacher's workshop. *Journal of the Royal College of General Practitioners*, **22**, 551–559.

Pietroni, P. C. (1984) Training or treatment – a new approach. *British Journal of Holistic Medicine*, **1**, 109–112.

Sowerby, P. (1977) *The Doctor, His Patient and the Illness:* a re-appraisal. *Journal of the Royal College of General Practitioners*, **27**, 583–589.

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Book Reviews

Editor: Sidney Crown

Enriching Heredity: The Impact of the Environment on the Anatomy of the Brain. By Marion Cleeves Diamond. New York: The Free Press. 1988. 191 pp. $24.95.

Darwin noticed that the brains of domestic rabbits were smaller than those of wild rabbits, and attributed this to lack of stimulation. Ramon y Cajal, in 1911, suggested that mental activity might increase the number and connections of brain cells. Hebb, in 1948, found that pet rats were better than caged rats at solving mazes and suggested that this was due to the effect of increased stimulation on the brain. Such observations and ideas raise the question of whether brain power can be increased by appropriate environmental stimuli, and one way to study this is to see if differences in experience are associated with differences in brain structure.

Enriching Heredity summarises some 25 years of research by Diamond and her team at the University of California, Berkeley. Their principal concern was to measure cortical thickness in the brains of experimental rats, comparing the effect of environmental enrichment (plenty of space, play-mates, mazes, toys) with impoverishment (small cage, isolation) and with normal laboratory conditions. They found that the thickness of the occipital cortex was some 7% greater in enriched than in impoverished rats, and that this increase was principally in those layers (II and III) which are last to develop and which therefore probably retain the greatest plasticity. Enrichment was also associated with an increase in the size (although not the number) of neurones, in the number of dendritic branches, in the extent of synaptic thickening, and in the proportion of glial cells (a proportion which generally reflects the complexity of the brain, and which was particularly high, they found, in a sample of Einstein's brain). They also showed (and say they were the first to do so) that enriched conditions for parents or pregnant mothers were associated with increased cortical thickness in the offspring, and that in female rats, cortical thickness was increased both by pregnancy and by ovariectomy. Other studies related cortical thickness to sex hormones, the immune system, and ionic charges in the air.

How far such findings may have relevance for the human brain is uncertain, but they allow some interesting speculations. After puberty, rats did not lose any significant numbers of cortical cells, even in old age, and this might make us wonder whether the adult human brain really loses 100 000 neurones a day (as is widely believed). In rats, age is no bar to the increase in cortical thickness and maze-learning ability which follow environmental enrichment, and this might suggest that "the use of our nerve cells is critical to their continued health". In very old rats, enrichment is associated not only with cortical increase but with diminished life expectancy; this might be due to the stress of having play-mates and so suggest an increasing need for solitude in the elderly.

It is a pity then that this book, of such potential interest, is almost impossible to read. The style is flat, and the text too much taken up with detailed description of experimental procedures. There are no convenient summaries of the findings, and no account of how the team's work relates, over the years, to the findings of other workers in this subject. No mention is made of Hubel and Wiesel, who were perhaps the first to show that the structure of the cerebral cortex could be influenced by sensory experience. The non-specialist reader, interested to know if nurture can improve the innate capacity of the human brain, may well feel like a tyro at a gold mine – a lot of panning is needed for a few nuggets.

Edward Hare, *Emeritus Psychiatrist, 47 Alleyn Road, London*

Behavioural Medicine in Cardiovascular Disorders. Edited by T. Elbert, W. Langosch, A. Steptoe and D. Vaitl. Chichester: John Wiley. 1988. 328 pp. £39.50.

This book is a compilation of papers that the editors hope outline recent cardiovascular research relevant to behavioural medicine. Many of them were presented at a European conference in 1985, and most of the contributors are European, although there have also been some invited submissions from American workers.

The book is divided into four sections, looking at the psychophysiology of hypertension, behavioural management of hypertension, coronary heart diseases, and cardiac arrhythmias. As with most multi-author books, the different chapters are extremely varied, some being complex and hard to follow, but others being of extreme interest. Of particular interest is an article by Dworkin on his novel psychosomatic hypothesis for the cause of hypertension. He outlines a possible relationship between reduction of pain and development of raised blood pressure, and provides some research data to support his theory. Chapters by Pickering and Steptoe, reviewing psychological aspects of the aetiology and treatment of hypertension, are also of considerable merit. Roskies presents a clear description of a stress management programme for altering type 'A' behaviour, and there is a useful review of the cardiovascular aspects of panic disorders from Ehlers *et al.*

Unfortunately, interspersed with these useful chapters are a number of very complex articles, and the overwhelming impression gained from the book is that there is still a considerable amount of work to be done in this area to clarify the contribution that behavioural medicine will make in the future to both determining the cause of and treatment of various cardiovascular disorders. Those who specialise in this area will wish to read this book, although the general psychiatrist is less likely to find it useful.

CHRIS THOMAS, *Consultant Psychiatrist, Department of Psychiatry, County Hospital, Hereford*

Borderline and Narcissistic Patients in Therapy. Edited by NONNA SLAVINSKA-HOLY. Madison, CT: International Universities Press. 1988. 515 pp. $50.00.

This 23 chapter, multi-author collection includes accounts of many sorts of therapies with patients classified broadly under the title headings. Individual and group treatments of various sorts are described, together with marital and family work, active techniques, and therapeutic community approaches. Departure from a strict analytic stance is widely advocated for these patients, and even at times the concurrent use of drugs by the therapist. Perhaps inevitably in a work that attempts to be this broad, there seems to be some confusion over the term 'borderline', which is used over-inclusively. For example, Ulman's fascinating description of an individual therapy, Sacks' account of a psychodrama treatment, and Astigueta and Verhaests' accounts of therapeutic communities, although all clinically compelling, do not seem to be talking about the same sorts of patients at all. This may be off-putting to a British readership already suspicious of the term.

Although we are told in the preface that a cross-section of views by leading practitioners will be represented, the frame of reference is mostly Kohutian 'self-psychology'. Rosenfeld is barely mentioned, Steiner does not appear in the index, and Kernberg is brought in mostly to be disputed. It is made clear, however, that the emphasis is clinical, without a systematic literature review or theoretical critique. As the editor says, these disorders are currently at the centre of professional attention. Borderline and narcissistic patients are grouped together because of the similarities in their primitive defences, and what is termed their shared problem of lack of authentic identity. In the Kohutian sense, they lack integration in mental structures rather than having structural conflicts. We are told that dualistic and instinctual positions have given way to holistic and integrative ones, and that what will be stressed here is "a view of the psychotherapist as a human being working in a joint energic-affective field with the patient". To my taste, this sort of language, which does recur, jars somewhat and lacks precision. However, a wealth of fascinating clinical material is presented, and the chapters by Pines and Hearst are a refreshing contrast in that they both give cogent presentations of self-psychology in theory and in group practice which are eminently readable.

A thread running through the book is a plea for the therapist to examine his own part, particularly his own failures, in the therapeutic relationship. Also stressed is a model of fostering the positive transference, and of allowing the use of the therapist as a mirroring or idealised 'self object'. Although the mechanisms of splitting and projective identification are frequently referred to as important, it is not often clear how they are used clinically in the presentations, which suffer generally from a lack of detailed description of the transference and countertransference phenomena encountered with these difficult patients.

With these reservations, I think this will be a useful text for the reader with an interest in self-psychology, particularly in view of the richness of clinical material presented. It should be available in libraries to be dipped into by anyone working psychotherapeutically with disturbed patients.

JANE MILTON, *Senior Registrar in Psychotherapy, The Maudsley Hospital*

Psychological Assessment of the Elderly. Edited by JOHN P. WATTIS and IAN HINDMARCH. Edinburgh: Churchill Livingstone. 1988. 201 pp. £29.50.

This book is the latest in a series taking a specialist view of the psychiatry of old age. The contributors are all acknowledged experts in their field, and the book covers the wide range of measurements of mood and behaviour available in the elderly, from the psychological approach, through questionnaires and computer-based assessments, to an evaluation of the use of psychotropic agents. There is an excellent chapter discussing the reliability and validity of scales and the particular difficulties associated with their use in the elderly. The vexed question of what is normal in mental health terms in the elderly is also thoroughly discussed. The chapters on the various scales have been prepared by different authors, leaving the reader a little confused at times over the merits of one particular scale over another, but the theoretical discussions are well backed up by examples of research projects where the various scales have been road-tested.

The chapter on psychological approaches to the assessment and treatment of old people stands out as the most useful for the practising rather than research-orientated psychiatrist, and is full of interesting case vignettes.

One significant omission is an investigation of the usefulness of suicidal intent scales in the elderly, but otherwise this is a well-written and useful addition to the psychiatric literature and deserves a place on all hospital library shelves. It is a book to be dipped into rather than read at one sitting.

MIKE NOWERS, *Consultant Psychiatrist with Special Responsibility for the Elderly, Frenchay Health Authority*

Justice Unbalanced: Gender, Psychiatry and Judicial Decision. By HILARY ALLEN. 151 pp.

This is a relatively short book (six chapters and a conclusion), the brevity disguising the depth and intricacy of the author's exposition and analysis of the source material. A wealth of case material is examined, and Allen manages a good balance of quotes, comment and analysis.

Chapter two rehearses the legal arguments and traces the inconsistency and contradictory nature of reasonableness and diminished responsibility as it relates to gender, arguing that this is the first stage at which decisions affecting gender are made. Chapter three makes a detailed examination of the reports available, and discusses the differences between men and women in the verdicts reached: 24 males (3 diminished responsibility) and 22 females (6 diminished responsibility, 3 infanticide, one unfit to plead).

The chapter on the development of the prison medical service – its subservience to the 'system', followed by a period of ascendency, with a regrettable return to the earlier position – makes fascinating reading. There is also an explanation for the difference between the provision of psychiatric services in men's and women's prisons, reflected not only in regimes but more crucially in the reports prepared for the Courts. Why is it that psychiatry seems reluctant to diagnose, let alone treat, a majority of the men whom the Courts confidently identify as 'mental cases'?

In conclusion, this is not a book to browse through, but to read at one sitting. Its examination of the case records is illuminating, and has certainly urged me to examine my own practice (especially as I recognise some of my own cases in the text!). The book has, unusually for the topic, avoided the superficial and 'obvious' explanations and treated us to a far deeper set of interpretations. While there is undoubtedly a disproportionate 'psychiatrisation' of women, the author is more concerned at the underuse of psychiatry for males. In her own words, "Contrary to my initial political prejudices, which saw the excess of psychiatry as personally oppressive to female offenders, it became increasingly clear as the analysis progressed that on the whole, female offenders do rather well out of it".

PETER HODGKINSON, *Probation Officer, After Care Unit, Inner London Probation Lecturer in Criminology and Penology, Faculty of Law, Polytechnic of Central London*

Dream Fulfillment. Edited by MARIA C. GEAR, ERNESTO C. LIENDO and LILA L. SCOTT. Northvale, NJ: Jason Aronson. 1988. 230 pp.

This book is an attempt to do for the patient what Joseph did for the Pharaoh – the use of dreams to plot the future. The authors, who root their authority in psychoanalysis, should have heeded Freud's warning on this at the Berlin conference in 1920. They argue that patients develop "telemelodramas" or addictions to escape anxiety. The function of the therapist is to interpret away these defences so that they can have "reachable dreams". All this is wrapped up in a heavy dose of pseudobiology rampant with "left digital highlanders" and "right analogic lowlanders" living in "Krantzland" (Manhattan). It is an excellent example of what Thomas Szasz has called the use of language to mystify and discredit types of behaviour by the use of disparaging neologisms, and the reformulation of types of behaviour into acceptable rhetoric.

This book, aimed explicitly at the Manhattan market, is strictly for California dreamers and their disciples. Those who practice in the waking state may find the going soporific.

L. RATNA, *Consultant Psychiatrist, Barnet General Hospital, Wellhouse Lane, Barnet, Herts*

The Chronic Mental Patient/II. Edited by W. WALTER MENNINGER and GERALD HANNAH. Washington DC: American Psychiatric Press (distributed in the UK by CUP). 1987. 255 pp. £18.50.

Psychiatric Rehabilitation of Chronic Mental Patients. Edited by ROBERT PAUL LIBERMAN. Washington DC: American Psychiatric Press (distributed in the UK by CUP). 1988. 341 pp. £17.50.

These two books are respectively the proceedings of a multidisciplinary conference, and what might be termed the companion to a regularly held workshop for health professionals. Both are multi-author works, and both cover some similar ground. However, the former focuses on epidemiology, politics, resources, and so on, while the latter concentrates on diagnosis, functional assessment, and approaches to treatment.

In style, the first book inclines to the academic and detached. The discussions on prevalence of chronic mental illness, homelessness, and social and political aspects are all to a greater or lesser extent thorough, scholarly, and well referenced. The second book essentially outlines an aggressive, but not particularly innovative, treatment approach in an enthusiastic fashion. There are chapters on practical psychopharmacology, social skills training, family management, vocational rehabilitation, and community support. Flow diagrams, case histories, and learning exercises abound, but references are thin on the ground.

These books are aimed at an American readership: the social, political, and economic contents of the first do not always have obvious counterparts in Britain, and the uncritical style of the second will grate on many British psychiatrists. Perhaps the most striking feature of both books is an optimism about chronic mental illness, particularly chronic schizophrenia. Accordingly, they will both undoubtedly be welcomed by community-orientated psychiatrists, but will perhaps meet with a more weary scepticism from the remainder.

P. J. McKenna, *Lecturer in Psychiatry, University of Leeds*

Human Behaviour in the Concentration Camp. By Elie A. Cohen. London: Free Association Books. 1988. 295 pp. £9.95.

Cohen is a Dutch physician, one of the 60 000 Jews deported from the Netherlands to Auschwitz and one of only 1052 who survived. Eight years after his liberation he presented a thesis for a Doctorate of Medicine, which was published in book form in 1954. The book is now reissued to fulfil the need of the author to constantly remind the world of "the depths of misery, madness and cruelty to which man is capable of descending".

The author acknowledges that the writing of this book arose out of a profound personal necessity, as part of his attempt to mourn his lost world. At the same time, he has tried to provide an objective account of the process. It is this combination which makes the book so overwhelming in its effect. Accounts of medical procedures and survivors' memories are interspersed with tables of statistics detailing the calorie content of a prisoner's diet or the ratios over the years of deaths to admissions. Cohen struggles, largely using psychoanalytic theory, to make sense of what happened. After dealing with general and medical aspects of the concentration camps, the remainder of the book is an attempt to deal with the psychology of the prisoner and of the SS guards. He admits that his own contribution to providing an explanation is limited, using medical psychology as his only tool, and that clearly other fields of study are required to really understand the behaviour and beliefs of an organisation such as the SS.

One can ask, almost half a century on, whether we still need reminding of the horror that existed in Europe. The answer must be yes, partly for its own sake, because it is our immediate history and part of us all, but also because it is only through this reminding that we really can be aware of the capacity of humans for evil. The terrifying thought is how much easier it would all be now with stainless steel equipment, computerised records and more effective and 'humane' despatch methods. It is not a pleasure to read this book. It is a duty.

Stephen Wolkind, *Consultant Child Psychiatrist, Children's Department, The Maudsley Hospital*

Reclaimed Powers: Towards a New Psychology of Men and Women in Later Life. By David Gutmann. London: Hutchinson Education. 1988. 335 pp. £30.00.

This engrossing book is clearly the summation of a career in gerontology, but the contents are endowed with additional relevance and intimacy by Gutmann's comment that his own ageing is "a prime object of my study".

Gutmann opposes the view of old age as a period of involution and decay prior to death; he argues that it should be considered as a developmental stage in its own right. This assertion is supported by projective material, mainly obtained using the Thematic Apperception Test, collected from a variety of societies: urban Kansas, the Navajo of North America, the Highland and Lowland Maya of Mexico, and the Druze of Galilee and the Golan Heights. He found a recurring pattern in all the groups: that as they age, men become more 'feminine', whereas women become more 'virile'. He argues that this pattern fits in with the "parental imperative" and the need for differentiated gender roles during child-rearing; the declining aggression of men in old age allows their sons to assume power, aided by their wives, without conflict between the generations.

Industrialisation, urbanisation, and geographical mobility have arrested this pattern in contemporary Western society; Gutmann ascribes many present-day ills, including child abuse, to the ascendancy of the nuclear family. The book ends with a plea for a return to traditional social structures.

The book makes fascinating reading; each chapter is charmingly prefaced by an apposite literary quotation, a device which serves to remind one of the breadth and depth of learning underpinning Gutmann's work. I particularly enjoyed the chapter entitled 'The seasons of the senses', which deals with the return to orality of the older male. He also gives a fine account of the relationship between ageing and art.

Reclaimed Powers is perhaps misplaced in a series entitled *Handbooks for the Caring Professions*, as it is neither a practical guide nor exclusively of interest to a professional audience. The style and content make it approachable by the lay person, but the comprehensive appendix and notes should also make it acceptable to the professional.

JULIA PALMER, *Senior Registrar in Psychiatry, St George's Hospital, London.*

Treating Troubled Adolescents: A Family Therapy Approach. By H. CHARLES FISHMAN. London: Hutchinson. 1988. 330 pp. £25.00.

Adolescence is taken in this book to be a developmental stage in the life-cycle of the family as a whole, and a structural form of family therapy is used. The author has previously collaborated with Minuchin, in *Family Therapy Techniques* (1981), and this new book could be seen as an illustrative companion. The core consists of transcribed extracts of therapy sessions which deal with severe disturbances such as violent, suicidal, or runaway behaviour. Theory is not expanded to a great extent beyond the introductory chapters and subsequent linking material. This can lead to a sense of oversimplification – as for example in the brief discussion of adolescence as a 20th century phenomenon and a product of social need, and as in the definition of homeostasis. But it also relates to one of the virtues of the book itself, and of the therapeutic method it describes – it consists of a few simple but powerful ideas put to the test time and again, adhered to tenaciously while avoiding the temptation to follow complex developments for their own sake. The repeated emphasis is on attending to the context of the difficulties, finding and confirming areas of competence, and presenting options to the family, while in the immediate present of the therapy session aiming for decision and change.

The case extracts are central to the purpose of the book, and on the whole they succeed well in illustrating the author's approach. But this was not always so: I found the nuances of the American colloquial dialogue too subtle in some cases to be meaningful. The text is also longwinded at times, as otherwise simple and clear points are laboured and repeated – perhaps a product of the method!

The avowed aim of the therapy here is rapid effective change in the face of crises. As such, the clear and simple therapeutic approach will be found valuable by many in these heated situations. The book does provide insights, and there are some touching moments.

HUGH BARNES, *Consultant Child and Adolescent Psychiatrist, Department of Family Psychiatry, Bristol Royal Hospital for Sick Children.*

Directive Group Therapy: Innovative Mental Health Treatment. By KATHY L. KAPLAN. New Jersey: Slack. 1988. 165 pp.

Directive group therapy, in the author's own words, is "a special form of group treatment designed to meet the needs of acutely ill, minimally functioning patients ... [who are] unable to function in almost all areas and have serious impairment of communication and judgement capacities". These patients, on acute admission wards, get the benefit of intensive medical assessment and physical treatment, plus intensive nursing care, but are rarely seen as able to benefit significantly from group-orientated occupational treatments (OTs) because of their minimal functional capacity. This book describes, with admirable clarity, a programme designed to offer such treatment.

Occupational therapists have, in recent years, become much occupied with Kielhofner's model of human occupation, derived from systems theory, which aims to give a firm theoretical basis to the ways OTs work. This model provides a structure within which assessment, treatment, and monitoring of patient's needs, progress, and outcome are given meaning in terms of each individual patient's volition (using parameters of exploration/helplessness), habituation (competence/incompetence), and performance (achievement/inefficiency). Each of these are seen as part of a hierarchy of interacting subsystems, such that those levels which guide or constrain function at other levels can be addressed and modified directly. This model is clearly, albeit briefly, outlined in an early chapter of Kaplan's book, and informs much of the rest of the text.

Thereafter, the book is itself a model of how a difficult clinical problem can be addressed within a multidisciplinary team. It is essentially a practical handbook, describing how the author and her colleagues set up and ran their directive group programme (in a unit with enviably high multidisciplinary staffing levels!), but also providing guidance, advice, and instruction to others wishing to do the same. The practical chapters contain facsimiles of forms used for referral, initial assessment, and monitoring, which are in the main clear, brief, and directed to appropriate areas of function, and all sections are illustrated with case material. Whatever the style of therapy, these practical plans for assessment, setting goals, and monitoring treatment provide a useful model for most professionals involved in offering psychosocial treatments. How many OT departments have a wide range of 'accepted' treatments on offer, many in group settings, where this kind of practical approach to definition and evaluation of the function of the group would not be of benefit to patient care and reassuring to those of us in the multidisciplinary team who remain unconvinced of the value of loosely formulated interventions such as concentration or communication groups?

Directive group therapy (like much else that is offered to patients as part of a treatment package) has not been formally evaluated, and the author admits with disarming honesty that her evidence for its effectiveness is anecdotal. However, she makes a clear and welcome plea that such treatments be formally evaluated. Being an American book, some of the practical advice will be of little value to workers in the UK – for example, there are lists of useful American addresses from which to obtain materials to use in the group. Also, the writing style is that rather uncomfortable mixture of second-person 'buttonholing', occasional slang, and unnecessary jargon sometimes found in American texts that I, for one, find difficult to read. However, it is admirably short, and the content more than makes up for the style.

GRAEME MCGRATH, *Consultant Psychiatrist, Manchester Royal Infirmary*

The Sexual Relationship: An Object Relations View of Sex and the Family. By DAVID E. SCHARFF. London: Routledge. 1988. 268 pp. £8.95.

This volume is published as a part of a growing and impressive collection of works which make up the *International Library of Group Psychotherapy and Group Process*. Scharff is an American who spent time at the Tavistock Centre in the early 1970s. The British school of object relations theorists has had a profound influence on his thinking and practice. This is apparent throughout the book, and is reflected in the subtitle. In the development of his understanding of difficulties encountered in sexual relationships, Scharff has clearly also been influenced by Bowlby: a secure attachment to the mother or a difficulty in this area is understood to inevitably influence the ebbs and flows of sexual interactions.

Scharff views the sexual relationship as an interactive screen, found in the space between two individuals. This 'screen' attracts projections from each person's inner world, and consequently will reflect their capacities to develop, or needs to defend against, a creative partnership. Due to the variety of psychosomatic elements which are called into play in an encased sexuality, Scharff suggests that it is in this area that therapeutic links can be made between the formative years of each partner and the difficulties found in their external world of adult relationships. This point is illustrated through an abundance of case examples.

Scharff gives the reader access to his style of work as he explores his patients' earliest experiences: with the mother, with the parental relationship, and with the preoccupying themes in the family of origin. His main emphasis is on the interpretation of inner-world influences, particularly because these tend to be beyond the conscious reach of his patients. However, he does not overlook the impact of the more external factors such as naivety, lack of experience, and bodily realities such as dysfunction, ill-health, or aging. Scharff continually and helpfully stresses interactions: "At any given moment, the maturity of sexual relatedness is an achievement resting on the balance between the individual, his internal objects, and his external relationships."

There are times when the case examples are so plentiful that they become obscuring. However, overall this is a successful blend of theoretical statements and illustrative material. Scharff has a thorough and accomplished style which challenges the reader to think. His notation of reference material is particularly good, and provides a rich diet for further reading. There are even two appendices: one outlining the fundamentals of object relations theory, and the other the sex therapy treatment model he uses, which is based on Helen Kaplan's work. This book is a worthwhile read and is thoroughly recommended.

PETER FULLERTON, *Marital Psychotherapist, Tavistock Institute of Marital Studies, London*

The Anatomy of Madness. Essays in the History of Psychiatry. Vol III. The Asylum and its Psychiatry. Edited by W. F. BYNUM, ROY PORTER and MICHAEL SHEPHERD. London: Routledge. 1988. 353 pp. £35.00.

In reviewing the first two volumes of this series (*Journal*, September 1986, **149**, 389–390), I likened the contents to a literary lucky-dip with a prize for everyone who chances his arm. This third volume maintains the same standard of excellence, although I missed the punch-ups between different contributors holding opposing views on kindred subjects which were such an intriguing feature of the earlier volumes. The choice of subjects is wide-ranging, and anything but parochial in interest. Thus, there are essays relating to psychiatry in Denmark, British India, Italy, France, and America, apart from those appertaining to the UK.

From a personal and selfish point of view I welcomed David Cochrane's able and much-needed account of the London County Council (LCC) as administrators of Victorian lunacy policy. In actual fact, the hospitals controlled by the LCC up to the outbreak of the second world war ringed the metropolis like a bicycle wheel, with County Hall, the administrative power house, at the hub and the Maudsley, the think tank, a little off-centre. All together they provided a mental health service which, despite its rigid social stratification and its religious devotion to the book of rules, was efficient, prestigious, powerful, and seemingly as eternal as Imperial Rome. Of these things I know because, like so many of my generation, I served my psychiatric apprenticeship under its aegis.

For equally selfish reasons I enjoyed Richard Russell's chapter, because of its special reference to the West Riding Lunatic Asylum in Wakefield where, as a student at Leeds, I was richly entertained by the patients, mainly hypomaniacs, at what purported to be a clinical demonstration, but learned little or no psychiatry in the process.

Trevor Turner's contribution is to be strongly recommended to all those who would hope to gain some insight into that brilliant yet enigmatic psychiatrist/philosopher who dominated the British scene in the 19th and early 20th centuries – Henry Maudsley. Incidentally, Turner, a mere stripling in chronological terms, gives the lie to the somewhat snide allegations in the Introduction to Volume II that the history of psychiatry is "the almost exclusive preserve of elderly psychiatrists". It is true, alas, that the subject has been largely taken over by scholars in peripheral disciplines, but it could be that the establishment of a History of Psychiatry Group of the College will redress the balance.

The standard of scholarship overall is high, and the essays are rich in primary and secondary sources which have hitherto been under-researched. There is the occasional flaw, however. For example, Nancy Tomes (p.193) claims that the title of the journal of the Association of Medical Officers of Asylums and Hospitals for the Insane, first published in 1853, was the *Asylum Journal of Mental Science*. The title was, of course, *The Asylum Journal*, later to be changed to the *Journal of Mental Science*. Again, her claim that the poor attendance at early meetings of the Association was due to divisions between private madhouse doctors and those working in county asylums is only partially true. More to the point is the fact that asylum doctors were marooned in their isolated institutions which they often ran single-handed. For them to attend meetings in, say, London, Oxford, or Edinburgh was difficult if not impossible.

Nevertheless, a boxed set of all three volumes of the series would make an excellent gift to retiring consultant psychiatrists if, that is, the not inconsiderable monies involved were to be subscribed by sorrowing colleagues when the hat went round.

HENRY R. ROLLIN, *Emeritus Consultant Psychiatrist, Horton Hospital, Surrey*

Lithium Treatment of Manic Depressive Illness: A Practical Guide (4th edn). By M. SCHOU. Basel: S. Karger. 1989. 50 pp. £6.40.

This book had to be written. It is no exaggeration to talk of the "lithium revolution" of the 1970s. Few psychiatrists or general practitioners do not encounter manic depression in their everyday practice, and affective disorders are of major epidemiological significance. Likewise, most doctors have had to deal with patients who are inclined to take their own lives. The national suicide statistics are still frightening. Many of these individuals suffer from 'affective illness' of a recurrent or bipolar type, and are therefore potential candidates for lithium therapy or prophylaxis. Lithium is to manic depression as neuroleptics are to schizophrenia.

This thin volume is written by an acknowledged master of his craft. It is admirably brief – even terse. The language is simple layman's English, easy to understand and assimilate. The book is thus likely to become required reading for all who have to do with lithium – patients and carers alike. The notes on lithium, pregnancy, and breast feeding are particularly well done.

There are, however, minor blemishes. To whom is the book directed – patients or physicians? The note on the unwanted effects of neuroleptic-lithium combinations fails to discuss the reports of neurological sequelae. Although there is a section on renal function, there is no mention of the diabetes insipidus-like syndrome which may be irreversible in some cases. But these points apart, this book deserves to be widely circulated and read. The price is well within the reach of most pockets.

MICHAEL W. P. CARNEY, *Consultant Psychiatrist, Northwick Park Hospital and Clinical Research Centre, Harrow*

Organic Psychiatry: The Psychological Consequences of Cerebral Disorder (2nd edn). By ALWYN LISHMAN. Oxford: Blackwell Scientific. 1987. 745 pp. £25.00 (pb), £45.00 (hb).

Lishman was awarded a six-month visiting fellowship at Green College, Oxford, where he was able to update the first edition of his book in the Radcliffe Science Library Division of the Bodlean Library – a place well-known to him, since this was where he wrote his first clinical papers. The result is a larger and more comprehensive edition, trimmed in some areas but expanded in others such as dementia and his own particular interest, brain damage associated with alcoholism. Over the 10 years since the first edition was published, certain areas of organic psychiatry have expanded explosively, particularly as a result of the new techniques for brain imaging. Structural techniques such as nuclear magnetic resonance and functionally-orientated techniques such as positron emission tomography (PET) scanning have become more available, the latter as a research tool. Both are covered in their theoretical aspects, and indeed the early papers on PET scanning in schizophrenia are mentioned. However, these inevitable omissions do not in any way detract from this vast body of knowledge, presented with immense care and attention to detail in a form which is easily read. There must be a great many psychiatrists like myself who when problems in organic psychiatry emerge think to ourselves, "I must check Lishman". I personally have never found him wanting.

DONALD ECCLESTON, *Professor, Department of Psychiatry, University of Newcastle upon Tyne*

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Review Article

The Role of Electroconvulsive Therapy in the Treatment of Depressive Illness in Old Age

S. M. BENBOW

Electroconvulsive therapy is an important treatment in the depressive states of late life, and there is general agreement about the indications for its use in old age psychiatry. Indeed, old age may be associated with a better response to ECT than that in younger age groups. The additional risk involved through physical problems in the elderly is not great when compared with that of continuing depression and of the side-effects of alternative treatments. Temporary memory disorders and confusion may occur, but are minimised if unilateral electrode placement is used. Some patients treated with unilateral ECT do not respond, but will respond to bilateral treatment. Anxiety over unwanted treatment effects, which can lead to ineffective treatment of depressive illness, must be outweighed by knowledge of the dangers of leaving depression untreated in old age.

Electroconvulsive therapy (ECT) is used to treat a range of psychiatric disorders in younger people (Kendell, 1981), but in the elderly its use is virtually confined to patients suffering from serious mood disorders, particularly depressive states (Fraser, 1981). This can be considered in five sections.

(a) Which clinical features predict a good response to ECT?
(b) Do old people respond as well as younger patients to ECT?
(c) What physical problems are encountered in old people receiving ECT? Do any concurrent physical illnesses contraindicate ECT?
(d) What side-effects can be expected in old people treated with ECT?
(e) Are unilateral and bilateral treatments equally effective in the elderly?

Which clinical features predict a good response to ECT?

When ECT was first introduced its effect was so dramatic that it was not assessed by controlled trials. Post (1978), in his reflections on the major changes which had occurred during his professional lifetime working with mentally ill old people, describes how wards that had previously housed untreatable chronic melancholics were transformed by the possibility of resolution in response to treatment. Early enthusiasm for ECT led to its application in a wide range of clinical conditions.

The development of antidepressant drugs led to a review of the place of ECT in psychiatric treatment, and its role has become more clearly defined (Kendell, 1981). The evidence for the efficacy of ECT far outweighs any to the contrary, and now includes several controlled trials (Johnstone *et al*, 1980; West, 1981; Brandon *et al*, 1984). Although Lambourn & Gill (1978) found no difference between anaesthesia alone and anaesthesia plus brief pulse unilateral ECT, their study may be invalid because the stimulus they used may not have elicited effective convulsions.

Depression in late life remains a challenge for old age psychiatry, and prolonged morbidity is probably common in elderly depressives (Murphy, 1983; Baldwin & Jolley, 1986).

Several predictive scales have been developed from studies of people receiving ECT by relating response to treatment to initial symptoms. Unfortunately, comparison of the different scales is difficult because they were administered to populations of widely differing age structures. Abrams *et al* (1973) used three different scales, but found that none predicted outcome; they suggested that the reason for this could be that their sample included many older people, and age might alter the usual predictive features. Hobson (1953) had found earlier that presence of an obsessional previous personality was a significantly favourable feature, and was more common in those aged over 40 years.

Fraser & Glass (1980) studied 33 elderly depressed patients treated with ECT and, using a symptom check-list, compared the 12 patients who had responded best with the 12 patients who had responded worst. They found that patients who experienced good outcomes had higher scores on the scales for guilt, agitation, overall severity, depressed mood, psychic anxiety, and impaired work and interests. Duration of illness had been longer in the poorer-outcome patients. They concluded that in the elderly the degree of subjective mood change and associated symptoms are more important than the distinction between neurotic and endogenous depression.

Salzman (1982) arrived at a similar list of predictors of good outcome in his review paper, including guilt, loss of interests, agitation, anxiety, dysphoria, helplessness, worthlessness, somatic delusions, nihilistic delusions, and vegetative signs. He also regards longer duration of illness as predicting a poorer response. Gaspar & Samarasinghe (1982) regarded psychotic depression with delusions of nihilism, sin, and guilt, or hypochondriacal delusions as an indication for proceeding directly to ECT.

In summary, there is general agreement about the features which predict a good response to ECT, and these include many of the symptoms associated with the concept of 'endogenous depression'. Anxiety/agitation, which is said to be an unfavourable feature in the young (Hamilton, 1982), is linked with a good response in the old (Fraser & Glass, 1980; Salzman, 1982).

Do old people respond as well as younger patients to ECT?

Several texts assert that greater age predicts a better response to ECT; for example, "of all depressive syndromes those of later life react best to ECT" (Dally & Connolly, 1981), and "older patients are said to respond particularly well to ECT" (Fraser, 1981). What evidence is there to support this view?

Gold & Chiarella (1944) found that patients over 40 were more likely to improve with ECT than younger patients, with the best outcome in those aged 51–60 years (the oldest group they studied). Hobson's (1953) study produced a similar finding, with 48% of those over 40 making a good recovery compared with 36% of the younger patients. Roberts (1959) studied 40–60-year-old women treated with ECT, and found a tendency for older patients to have lower total symptom scores after treatment. This difference was not sustained at three-month follow-up, and was dismissed as due to small sample size ($n=50$).

Ottosson (1962) found that final outcome was independent of age, but that with increasing age therapeutic effect seemed to appear later, a finding that might be compatible with Godber's clinical impression that courses of ECT will often need to be much longer in the elderly (Godber, 1983). However, in a follow-up study, Godber *et al* (1987) used unilateral ECT as their preferred treatment, which may at least partly explain the longer courses.

Nystrom (1965) reported that young adults responded poorly to ECT. Mendels (1967) used a computer-derived method of relating clinical factors to the response of depressed patients to ECT, and found an association between improvement at three-month follow-up and age over 50 years, significant at the 5% level. Folstein *et al* (1973), in a retrospective study of 118 patients who had received ECT, also noted that the improvement was related to age: the improved group had a mean age of 50 years and the unimproved group a mean age of 31 years. Babigian & Guttmacher (1984) found that women aged over 75 years treated with ECT showed a substantially decreased mortality compared with non-ECT groups, suggesting that superiority for ECT compared with drug treatments in the elderly may not merely be short term.

From these studies the evidence suggests that older people "may actually have a better therapeutic response to ECT" (Weiner, 1982), but relatively few very old people have been studied. The psychopathology of depressive illnesses may differ at different ages, and it may be that to some extent the relationship depends on the propensity of the elderly to suffer from the sort of depressive illnesses that do respond well to ECT. For example, Baldwin (1988) found that delusional depressions in old age required more physical treatments, especially ECT and major tranquillisers.

Alternatively, a relationship between age and therapeutic outcome could depend on a change in seizure duration with age, although the evidence on this is conflicting. Maletzky (1978) demonstrated a clear relationship with age and that a good response occurred only with total seizure times of over 500 seconds. On the other hand, Shankel *et al* (1960) demonstrated a positive correlation between the patient's age and the number of initial convulsion failures, and between the patient's age and the average duration of the tonic period, and Weiner (1980) found that seizure threshold correlated positively with age, whereas seizure duration correlated negatively. The observation that seizure threshold also increases with the number of ECT sessions administered may be pertinent in treatment of recurrent depressive illness in the elderly (Abrams & Volavka, 1982).

What response rate can be expected in depressed old people? Two recent studies have reported similar initial recovery rates in psychogeriatric populations: Godber *et al* (1987) found 51% recovered and 23% much improved, and Benbow (1987) found 52% well and 28% improved.

What physical problems are encountered in old people receiving ECT?

A range of problems have been reported in elderly people receiving ECT, including anaesthetic-related muscle pain (Devine *et al*, 1964), dental fracture (Faber, 1983), intraperitoneal rupture of the bladder (Irving & Drayson, 1984), and fractures of the thoracic spine in unmodified treatment (Impastato & Almansi, 1943). Cerebral haemorrhage, coronary occlusion, aspiration pneumonia, and pulmonary embolism accounted for four fatalities during 20 000 administrations of ECT given over three years in Matthew & Constan's (1964) study. Even so, ECT is generally safe for the elderly, and may be safer than tricyclics in those with cardiac problems (Weiner, 1982).

Gaspar & Samarasinghe (1982) reported clinical experience with 33 elderly people who were given 384 sessions of ECT over three years. One patient accidentally cut her tongue, and another vomited during recovery. Two patients showed prolonged confusional states, which worsened after each session of ECT, but cognitive function was fully recovered within days of completing each course. Four of the 33 people died within the study period, two in the community after discharge from hospital. Of the two who died while in psychogeriatric care, one had failed to respond to ECT and pursued a deteriorating course to die of bronchopneumonia, and the other patient, who suffered from depression and dementia, fell, sustained a fracture, and died six months after recovering from the depressive illness.

Fraser & Glass (1980) found a low incidence of side-effects, with no difference between unilateral and bilateral treatments. Of their original 33 patients, one died of a chest infection, and another was transferred to a different hospital with a chest infection. Similarly, of Karlinsky & Shulman's (1984) 33 patients, one had repeated episodes of pneumonia during a course of ECT.

Elderly people who receive ECT tend to have many physical problems. Gaspar & Samarasinghe (1982) divided their patients into major, minor, and no risk cases on the basis of physical examination, past and present history, and investigations. Ten out of 33 patients had major and 15 had minor risk factors. Eight patients were free from risk factors and, of those, some had abnormal findings which were not regarded as constituting a risk. For the major risk group, ECT was very safe since no patient died of anaesthetic or ECT complications.

Vascular problems remain a concern for those prescribing ECT for the elderly. Gerring & Shields (1982) found that 40% of 42 patients treated with ECT had pre-existing cardiac disease, and of these, 70% developed signs of ischaemia or an arrhythmia during treatment. Four episodes were potentially life threatening. All cardiac complications occurred in those over 50, the majority in those over 60.

Medical problems arising during ECT are significantly more common in those aged over 65, and the most important of these are cardiovascular (Alexopoulos *et al*, 1984). A review of 30 patients aged 60 and over receiving ECT at another centre found that adverse events were concentrated in the oldest patients, and correlated with a general index of physical health; in particular, patients who developed complications were likely to have a history of cardiovascular disease (Burke *et al*, 1985). Serial electrocardiograms and serum cardiac enzyme concentrations in patients receiving ECT have not revealed any persistent changes (Dec *et al*, 1985), but caution is advised in those over 75, especially with known cardiovascular disease, and Gerring & Shields (1982) recommend additional precautions and close monitoring in patients at high risk of cardiac arrhythmias.

ECT has been used successfully and safely in patients with post-stroke depressive illnesses and active medical problems (Murray *et al*, 1986). Loo *et al* (1985) have described five successful courses of treatment in depressed people on anticoagulants. Atre-Vaidya & Jampala (1988) note that, where affective disorder and Parkinson's disease are present together, ECT may be the treatment of choice because of poor response to, or complications with, drug treatments.

The presence of dementia is not incompatible with the use of ECT (Perry, 1983; Benbow, 1985, 1988). Psychogeriatricians have not excluded patients who are demented as well as depressed from treatment (Godber *et al*, 1987; Benbow, 1987). Indeed, Salzman (1982) argues that, since memory impairment in dementia may be exacerbated by the memory loss associated with depressive illness, ECT may improve memory function in some demented old people with superadded depressive illnesses.

It seems that physical problems in old people receiving ECT are not a major difficulty when one considers how ill this group are both physically and mentally, and that untreated depressive illness is itself a more serious threat.

What side-effects can be expected in old people treated with ECT?

Effect on memory

Anterograde and retrograde amnesia appear early in a course of ECT and are cumulative, but with some recovery between treatments. The anterograde amnesia fades after completion of the course, and effectively disappears by six months. Retrograde amnesia also shrinks after completion of the course, to leave some permanent loss only for events occurring during the week or two before treatment. The depressive illness itself may at least partly contribute to this loss. Memory complaints are fairly common after ECT, and persist even when deficits can no longer be detected on testing. It is generally accepted that complaints are less after unilateral treatment (Squire, 1982).

Since cognitive impairment is more often found in elderly people, their memories are regarded as more vulnerable. As memory loss is greater after bilateral ECT than after unilateral non-dominant ECT, unilateral is often preferred in practice with the elderly (Salzman, 1982).

Fraser & Glass (1980) found that all their patients had impaired memory function when tested before ECT, but three weeks after ECT their scores had improved to within a normal range for their age. They could find no significant difference between unilateral and bilateral groups on testing. Raskind (1984) found no evidence of an interaction between patient's age and cognitive change following ECT. Autopsy findings on an 89-year-old who had received 1250 ECT treatments showed no evidence of brain injury (University of Louisville School of Medicine, 1985).

Confusion

Fraser & Glass (1978) examined nine patients who had been given a course of alternating bilateral and unilateral treatments, and found that the time to recovery of consciousness, respiration, and orientation was significantly slower after bilateral ECT. Bilateral ECT also showed a cumulative effect, in that the time for recovery was significantly prolonged after the last bilateral ECT of a course compared with the first. There was also an interval effect with bilateral ECT, in that recovery time was prolonged further if treatment was given after a one-day rather than a two-day (or more) interval. In contrast, unilateral ECT showed neither cumulative nor interval effects. The authors concluded that unilateral ECT is to be preferred, and did not alter this view despite a later study which did not demonstrate a cumulative effect with bilateral ECT (Fraser & Glass, 1980).

Psychotropic medication during ECT and prior major medical illness are factors which have been found to be important in the development of acute confusional state after ECT (Summers *et al*, 1979), and both are common in elderly populations treated with ECT.

One retrospective study (Alexopoulos *et al*, 1984) found that transient disorientation occurred in 12.6% of elderly patients given ECT, and another (Benbow, 1987) reported confusion in 24% of courses to elderly people.

Are unilateral and bilateral treatments equally effective in the elderly?

It has often been stated that unilateral ECT should be the rule in elderly patients because of the shorter recovery time and less memory impairment (Fontaine & Young, 1985). Heshe *et al* (1978) recommended unilateral ECT as the standard procedure unless the patient is female, over 60 years of age, and only mildly depressed, even though their results are capable of a contrary interpretation. In their study, the results with bilateral ECT were significantly better than with unilateral ECT one week after completion of treatment, but this difference had disappeared at three months. The authors relate this early discrepancy to the seven patients within their unilateral group who did not respond to treatment; in addition, seven out of the 51 patients were not assessed at three months. These results suggest that bilateral treatment is superior, at least in the short term.

Stroemgren (1973) also preferred unilateral ECT, because of the tendency for bilateral ECT to affect memory. She had found no difference in therapeutic efficacy, despite the fact that, in the 45–65-year age group, a comparable therapeutic effect had been achieved using significantly fewer bilateral ECT compared to unilateral ECT.

Fraser & Glass (1980) studied 33 elderly patients who were randomly assigned to unilateral or bilateral treatment, and who were assessed blindly through the course. No difference was found in the length of course or the decrease in Hamilton rating score. They concluded that unilateral ECT was preferable to bilateral, but it must be borne in mind that the population they studied may not have been typical of patients receiving ECT: a substantial proportion of their sample were out-patients, they were well enough to manage without psychotropic medication for 24 hours before treatment, and an average of only 6.5 treatments was necessary to achieve remission.

Salzman's (1982) clinical experience is that elderly patients who have not had ECT before will respond to shorter courses than will younger patients. He notes that some old people are resistant to treatment, especially if they have had ECT before, and suggests that this group will respond better to bilateral treatment. Overall he concludes that unilateral ECT is the treatment of choice, with the reservation that a trial of bilateral ECT is indicated if there is no response. Heshe *et al* (1978) also found a resistant group.

Price (1981) reported that 16 out of 35 depressed patients showed marginal or no response to unilateral ECT, but all subsequently responded well to bilateral. His non-responders were aged 31-83 years. He concludes that it is important not to discontinue treatment if there is no response to unilateral ECT, but rather to switch to bilateral treatment.

Abrams (1982) estimated the group of non-responders as 15-30% of endogenously depressed patients referred for ECT, but could not predict which patients would fail to respond. Mielke *et al* (1984) reported a similar proportion of non-responders; this group may have a higher proportion than expected of elderly people. Pettinati *et al* (1986) analysed the differences in efficacy between unilateral and bilateral ECT, and found a trend for older people to fare better with the latter. This could explain why findings vary between studies where the age profiles of recipients are dissimilar. Abrams (1986) suggested that this could explain the large therapeutic advantage for bilateral ECT in a study with a mean patient age of 51 years (Abrams *et al*, 1983).

Conclusions

(a) A wider variety of depressive illnesses in the old will respond to ECT, and anxiety/agitation is linked with a good treatment response.
(b) The elderly respond to ECT at least as well as younger people, and may even respond better.
(c) The elderly population treated with ECT have many physical problems, but in practice these do not interfere with the successful administration of treatment.
(d) Side-effects are not a major problem in the use of ECT. Theoretically memory problems should be more prominent after bilateral ECT, but this is not found clinically. Recovery time is prolonged after bilateral treatment, but there is no evidence that this is detrimental clinically.
(e) For many old people unilateral and bilateral ECT are equally effective in relieving depressive illness, but some will respond better to bilateral treatment, and these may have a history of previous response to bilateral ECT.

ECT clearly retains an important place in the armoury against severe depressive states in old age. In view of the continued chronic morbidity of depressive illnesses despite modern antidepressant drugs, it is important to review the use of the treatment in order to minimise the possibility of patients being denied effective treatment because of pre-occupation with temporary side-effects, exaggerated potential hazards, or media pressure.

References

ABRAMS, R. (1982) Technique of electroconvulsive therapy. In *Electroconvulsive Therapy: Biological Foundations and Clinical Applications* (ed. R. Abrams & W. B. Essman). Lancaster: MTP Press.

—— (1986) A hypothesis to explain divergent findings among studies comparing the efficacy of unilateral and bilateral ECT in depression. *Convulsive Therapy*, **2**, 253-257.

——, FINK, M. & FELDSTEIN, S. (1973) Prediction of clinical response to ECT. *British Journal of Psychiatry*, **122**, 457-460.

—— & VOLAVKA, J. (1982) Electroencephalographic effects of convulsive therapy. In *Electroconvulsive Therapy: Biological Foundations and Clinical Applications* (ed. R. Abrams & W. B. Essman). Lancaster: MTP Press.

——, TAYLOR, M. A., FABER, R., *et al* (1983) Bilateral versus unilateral ECT: efficacy in melancholia. *American Journal of Psychiatry*, **140**, 463-465.

ALEXOPOULOS, G. S., SHAMOIAN, C. J., LUCAS, J., *et al* (1984) Medical problems of geriatric psychiatric patients and younger controls during electroconvulsive therapy. *Journal of the American Geriatrics Society*, **32**, 651-654.

ATRE-VAIDYA, N. & JAMPALA, V. C. (1988) Electroconvulsive therapy in Parkinsonism with affective disorder. *British Journal of Psychiatry*, **152**, 55-58.

BABIGIAN, H. M. & GUTTMACHER, L. B. (1984) Epidemiologic considerations in electroconvulsive therapy. *Archives of General Psychiatry*, **41**, 246-253.

BALDWIN, R. C. (1988) Delusional and non-delusional depression in late life. Evidence for distinct sub-types. *British Journal of Psychiatry*, **152**, 39-44.

—— & JOLLEY, D. J. (1986) The prognosis of depression in old age. *British Journal of Psychiatry*, **149**, 574-583.

BENBOW, S. M. (1985) Electroconvulsive therapy in psychogeriatric practice. *Geriatric Medicine*, **15**, 19-22.

—— (1987) The use of electroconvulsive therapy in old age psychiatry. *International Journal of Geriatric Psychiatry*, **2**, 25-30.

—— (1988) ECT for depression in dementia. *British Journal of Psychiatry*, **152**, 859.

BRANDON, S., COWLEY, P., MCDONALD, C., *et al* (1984) Electroconvulsive therapy: results in depressive illness from the Leicestershire trial. *British Medical Journal*, **288**, 22-25.

BURKE, W. J., RUTHERFORD, J. L., ZORUMSKI, C. F., *et al* (1985) Electroconvulsive therapy and the elderly. *Comprehensive Psychiatry*, **26**, 480-486.

DALLY, P. & CONNOLLY, J. (1981) Electro-convulsion therapy. In *An Introduction to Physical Methods of Treatment in Psychiatry*. Edinburgh: Churchill Livingstone.

DEC, G. W., STEM, T. A. & WELCH, C. (1985) The effects of electroconvulsive therapy on serial electrocardiograms and serum cardiac enzyme values. A prospective study of depressed hospitalised in-patients. *Journal of the American Medical Association*, **253**, 2525-2529.

DEVINE, R., NEWTON, K. J. & SPEAR, F. G. (1964) Pain following ECT modified by muscle relaxants. *British Medical Journal*, *ii*, 1046-1048.

FABER, R. (1983) Dental fracture during ECT. *American Journal of Psychiatry*, **140**, 1255-1256.

FOLSTEIN, M., FOLSTEIN, S. & MCHUGH, P. R. (1973) Clinical predictors of improvement after electroconvulsive therapy of patients with schizophrenic, neurotic reactions and affective disorders. *Biological Psychiatry*, **7**, 147–152.

Fontaine, R. & Young, T. (1985) Unilateral ECT: advantages and efficacy in the treatment of depression. *Canadian Journal of Psychiatry*, **30**, 142–147.

Fraser, R. M. (1981) ECT and the elderly. In *Electroconvulsive Therapy: An Appraisal* (ed. R. L. Palmer). Oxford: Oxford University Press.

—— & Glass, I. B. (1978) Recovery from ECT in elderly patients. *British Journal of Psychiatry*, **133**, 524–528.

—— & —— (1980) Unilateral and bilateral ECT in elderly patients: a comparative study. *Acta Psychiatrica Scandinavica*, **62**, 13–31.

Gaspar, D. & Samarasinghe, L. A. (1982) ECT in psychogeriatric practice – a study of risk factors, indications and outcome. *Comprehensive Psychiatry*, **23**, 170–175.

Gerring, J. P. & Shields, H. M. (1982) The identification and management of patients with a high risk for cardiac arrhythmias during modified ECT. *Journal of Clinical Psychiatry*, **43**, 140–143.

Godber, C. (1983) Depression in old age. *British Medical Journal*, **287**, 758.

——, Rosenvinge, H., Wilkinson, D., *et al* (1987) Depression in old age: prognosis after ECT. *International Journal of Geriatric Psychiatry*, **2**, 19–24.

Gold, L. & Chiarella, C. J. (1944) The prognostic value of clinical findings in cases treated with electric shock. *Journal of Nervous and Mental Disease*, **100**, 577–583.

Hamilton, M. (1982) Prediction of the response of depressions to ECT. In *Electroconvulsive Therapy: Biological Foundations and Clinical Applications* (ed. R. Abrams & W. B. Essman). Lancaster: MTP Press.

Heshe, J., Roeder, E. & Theilgaard, A. (1978) Unilateral and bilateral ECT. A psychiatric and psychological study of therapeutic effect and side effects. *Acta Psychiatrica Scandinavica* (suppl. 275).

Hobson, R. F. (1953) Prognostic factors in electroconvulsive therapy. *Journal of Neurology, Neurosurgery and Psychiatry*, **16**, 275–281.

Impastato, D. J. & Almansi, R. J. (1943) A study of over two thousand cases of electrofit treated patients. *New York State Journal of Medicine*, **43**, 2057–2064.

Irving, A. D. & Drayson, A. M. (1984) Intraperitoneal rupture of the bladder and ECT. *British Medical Journal*, **288**, 194.

Johnstone, E. C., Deakin, J. F. W., Lawler, P., *et al* (1980) The Northwick Park electroconvulsive therapy trial. *Lancet*, *i*, 1317–1320.

Karlinsky, H. & Shulman, K. T. (1984) The clinical use of electroconvulsive therapy in old age. *Journal of the American Geriatrics Society*, **32**, 183–186.

Kendell, R. E. (1981) The present status of electroconvulsive therapy. *British Journal of Psychiatry*, **139**, 265–283.

Lambourn, J. & Gill, D. (1978) A controlled comparison of simulated and real ECT. *British Journal of Psychiatry*, **133**, 514–519.

Loo, H., Cuche, H. & Benkelfat, C. (1985) Electroconvulsive therapy during anticoagulant therapy. *Convulsive Therapy*, **1**, 258–262.

Maletzky, B. M. (1978) Seizure duration and clinical effect in electroconvulsive therapy. *Comprehensive Therapy*, **19**, 541–550.

Matthew, J. R. & Constan, E. (1964) Complications following ECT over a three-year period in a state institution. *American Journal of Psychiatry*, **121**, 1119–1120.

Mendels, J. (1967) The prediction of response to electroconvulsive therapy. *American Journal of Psychiatry*, **124**, 153–159.

Mielke, D. H., Winstead, D. K., Goethe, J. W., *et al* (1984) Multiple monitored electroconvulsive therapy: safety and efficacy in elderly depressed patients. *Journal of the American Geriatric Society*, **32**, 180–182.

Murphy, E. (1983) The prognosis of depression in old age. *British Journal of Psychiatry*, **142**, 111–119.

Murray, G. B., Shea, V. & Conn, D. K. (1986) Electroconvulsive therapy for poststroke depression. *Journal of Clinical Psychiatry*, **47**, 258–260.

Nystrom, S. (1965) On relation between clinical factors and efficacy of ECT in depression. *Acta Psychiatrica Scandinavica* (suppl. 181).

Ottosson, J-O. (1962) Electroconvulsive therapy of endogenous depression: an analysis of the influence of various factors on the efficacy of the therapy. *Journal of Mental Science*, **108**, 694–703.

Perry, G. F. (1983) ECT for dementia and catatonia. *Journal of Clinical Psychiatry*, **44**, 117.

Pettinati, H. M., Mathisen, K. S., Rosenberg, J., *et al* (1986) Meta-analytical approach to reconciling discrepancies in efficacy between bilateral and unilateral electroconvulsive therapy. *Convulsive Therapy*, **2**, 7–17.

Post, F. (1978) Then and now. *British Journal of Psychiatry*, **133**, 83–86.

Price, T. R. P. (1981) Unilateral electroconvulsive therapy for depression. *New England Journal of Medicine*, **304**, 53.

Raskind, M. (1984) Electroconvulsive therapy in the elderly. *Journal of the American Geriatrics Society*, **32**, 177–178.

Roberts, J. M. (1959) Prognostic factors in the electroshock treatment of depressive states 1. Clinical features from history and examination. *Journal of Mental Science*, **105**, 693–702.

Salzman, C. (1982) Electroconvulsive therapy in the elderly patient. *Psychiatric Clinics of North America*, **5**, 191–197.

Shankel, L. W., Dimassimo, D. A. & Whittier, J. R. (1960) Changes with age in electric convulsion reactions in mental patients. *Psychiatric Quarterly*, **34**, 284–292.

Squire, L. R. (1982) Neuropsychological effects of ECT. In *Electroconvulsive Therapy: Biological Foundations and Clinical Applications* (ed. R. Abrams & W. B. Essman). Lancaster: MTP Press.

Stroemgren, L. S. (1973) Unilateral versus bilateral electroconvulsive therapy. *Acta Psychiatrica Scandinavica* (suppl. 240).

Summers, W. K., Robins, E. & Reich, T. (1979) The natural history of acute organic mental syndrome after bilateral electroconvulsive therapy. *Biological Psychiatry*, **14**, 905–912.

University of Louisville School of Medicine (1985) 1250 electroconvulsive treatments without evidence of brain injury. *British Journal of Psychiatry*, **147**, 203–204.

Weiner, R. D. (1980) ECT and seizure threshold: effects of stimulus waveform and electrode placement. *Biological Psychiatry*, **15**, 225–241.

—— (1982) The role of electroconvulsive therapy in the treatment of depression in the elderly. *Journal of the American Geriatrics Society*, **30**, 710–712.

West, E. D. (1981) Electroconvulsive therapy in depression: a double-blind controlled trial. *British Medical Journal*, **282**, 355–357.

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French Empirical Criteria for the Diagnosis of Non-Affective Non-Organic Psychoses

Comparison between the criteria suggested by Professors Pull and Pichot and those of DSM–III–R

ALEXANDER M. P. KELLAM

At the end of the 19th century, when the current psychiatric diagnostic concepts used in most countries were being elaborated, in Germany particularly by Kraepelin, French-speaking psychiatrists, who until then had dominated European psychiatry, continued to develop their own system. This difference in classification is most apparent in the non-organic, non-affective psychoses. Although some of the French names used may be unfamiliar to anglophones, when the new 'consensus' criteria developed by Professors Pull and Pichot are compared with the DSM–III–R criteria it becomes apparent that the French and American concepts are converging.

In 1982 Professor P. Pichot discussed the diagnosis and classification of mental disorders in the French-speaking countries, drawing particular attention to the two categories of Transitory Delusional States (*Bouffée Délirante* etc.) and Chronic Delusional States. He regarded these categories as unique to the French system. (The French classification is by the Institut National de la Santé et de la Recherche Medicale (INSERM), 1969.) In the introduction of his 1982 paper, Professor Pichot said: "Because these two uniquely French nosological concepts overlap with several standard psychiatric entities, there can probably be no one-to-one correlation between French and other recognised nomenclatures although, as will be shown, almost identical criteria for some of the conditions they circumscribe are found in the latest classifications. . .".

He compared *Bouffée Délirante* with the then current DSM–III categories 295.4, Schizophreniform Disorder; 298.9, Atypical Psychosis; 298.3, Acute Paranoid Disorder; and 298.8, Brief Reactive Psychosis; and commented that this last category corresponded exactly to the French Reactive Bouffée Délirante. With regard to the Chronic Delusional States, he pointed out that the INSERM classification used the degree of delusional spread as an important differentiating factor; this is a distinctive feature of the French system. He compared these with the DSM–III categories 297.1, Paranoia; and 297.3, Shared Paranoid Disorder. Finally, he commented: "The hallmark of French psychiatric diagnosis and classification consists of criteria restricting the diagnosis of Schizophrenia and a corresponding increase in the number of non-schizophrenic delusional states reported." He added that the INSERM classification ". . . is an outline of diagnostic terminology without adequate discriminating definitions. This leaves extraordinary leeway for divergent diagnoses of a single disorder."

In this paper he also commented on the small but significant semantic differences between the French concept of *Délire* and its English translation, Delusion, and between the uses of the word 'Paranoid(e)' and its derivatives in the two languages.

Later, Professors M. C. and C. B. Pull and Pichot (1987*a*,*b*) described how they had developed empirical criteria for defining the French diagnostic categories of Non-Organic, Non-Affective Psychoses, drawing on the experience of a group of 87 senior French psychiatric specialists. They started by using an instrument called "The integrated lists of criteria for the taxonomic evaluation of non-affective psychoses" (LICET–S), which they had developed in 1981.

They asked each participating specialist to choose five of his or her patients who had received the diagnosis of Chronic Schizophrenia, Chronic Delusional Psychosis or Acute Delusional Psychosis, and for each patient to indicate the presence or absence of each feature in their list of 70 criteria. Chronic Schizophrenia, Chronic Delusional Psychoses, and Acute Delusional Psychoses are the three primary diagnostic groups dividing the non-affective non-organic psychoses in the French (INSERM) classification.

Group 02, Chronic Schizophrenias, contains eight subtypes, not dissimilar to those found elsewhere.

Group 03, Chronic Delusional States, contains five subtypes:

03.0 Paranoid or Non-Focused Chronic Delusional States
03.1 Focused Chronic Delusional States (of jealousy or being wronged), *"Délires passionnels et de Revendication"*
03.2 Chronic Hallucinatory Psychoses.
03.3 Imaginative Delusional States (in the sense of fantastic and made up as the patient goes along), *"Paraphrénie Fantastique ou Confabulante"*
03.4 Senile
03.9 Unclassifiable

Group 04, Acute Delusional States and Confusional States, also contains five subtypes. The first, 04.0, is called Acute Delusional State Considered to be Schizophrenic. The next two, 04.1 and 04.2, are the *Bouffées Délirantes*. The last two, 04.3 and 04.4, are called Confusional States, and they, like the *Bouffées Délirantes*, are divided into reactive and non-reactive types.

On initially analysing their results for each of the large diagnostic groups, Professors Pull and Pichot retained as absolute criteria only those symptoms which appeared in at least 82.5% of cases and as relative criteria only those appearing in 75%. They did not differentiate between relative and absolute for the non-symptom criteria, but retained these only if there was total agreement. The only exceptions to this were the criteria for age of onset. In this way, in the first paper (1987*a*) they developed four sets of empirical criteria, for Chronic Schizophrenia, Chronic Hallucinatory Psychosis, Chronic Delusional Psychoses (described as *Les Délires Chroniques Interprétifs* in French), and *Les Bouffées Délirantes*.

These first four sets of criteria were then sent to each psychiatrist participating in the study, and comments and suggestions were requested. With the help of these, Professors Pull and Pichot refined the criteria and produced more rigorous operational versions, which they were able to integrate into a decision tree. These final criteria were based on 104 cases of chronic schizophrenia, 83 cases of chronic delusional state and 52 cases of acute delusional psychosis. At this stage the authors also added a fifth category: Acute Delusional States Considered to be Schizophrenic.

These groups are compared with the DSM-III-R criteria (American Psychiatric Association, 1987) in Table I.

Chronic Schizophrenia

The French criteria suggested for Chronic Schizophrenia are as follows.

A. At least two of the following three manifestations for at least two months.

A1. *Severe disturbance of the train of thought.* At least one of the following:

(a) loosening of associations, i.e. thinking characterised by speech or ideas passing from one subject to another with little or no association between them
(b) thought blocking, i.e. interruption of a flow of conversation before the thought or idea is completed.

A2. *Severe affective disturbance.* At least one of the following:

(a) inadequate or inappropriate affect, obviously not in accord with the contents of speech or thought
(b) ambivalent affect, the simultaneous existence of contradictory affects about the same object.

A3. *Major alteration of the experience of reality.* At least one of the following:

(a) depersonalisation and/or derealisation
(b) delusional ideas of any type.

B. Permanent signs of the illness for at least six months, with the constant presence of both B1 and B2.

B1. At least one of the manifestations A1, A2 or A3 above or at least two of the following manifestations:

(a) speech vague, digressive, over-elaborate, circumstantial or metaphorical
(b) marked poverty of the content of speech
(c) affect blunted or flattened
(d) thinking bizarre (French *déréelle*), described (Pelicier, 1976) as "mental processes opposed to or in contradiction to the common experience of reality, illogical, bizarre, magical, or with a delusional colouring" (author's translation)
(e) behaviour bizarre or severely disorganised.

TABLE I
Comparison of INSERM and DSM-III-R classifications

INSERM	*DSM-III-R*
02.0–02.9 Chronic Schizophrenia	295.1–295.3, 295.6, 295.9 Schizophrenia
03.0, 03.1, 03.3 Chronic Delusional States (Chronic Interpretative Psychoses)	297.1 Delusional (Paranoid) Disorder
03.2 Chronic Hallucinatory Psychosis	–
04.0 Acute Delusional State Considered to be Schizophrenic	295.4 Schizophreniform Disorder – without many 'good prognostic features' present
04.1, 04.2 Bouffées Délirantes	295.4 Schizophreniform Disorder – with several 'good prognostic features' present 298.0 Brief Reactive Psychosis[1]

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1. Brief Reactive Psychosis is the only member of the earlier ICD-9 categories 298 which is still represented in DSM-III-R.

B2. At least one of the following manifestations:
- (a) deterioration, since the start of the illness, of the level of professional, domestic or scholastic functioning
- (b) deterioration since the start of the illness of social relationships.

C. Age of onset less than 40 years.

D. Acute delusional psychosis excluded.

E. Organic state, alcoholism and drug abuse excluded.

F. When the criteria in A and B are present but not for sufficient time, a diagnosis of probable Chronic Schizophrenia may be made.

G. Affective states are excluded.

When comparing this concept with the DSM-III-R criteria for Schizophrenia, one can see that both demand a fairly prolonged illness, although the duration of the critical psychotic symptoms in the DSM-III-R criteria only needs to be one week whereas it is two months in the French criteria.

The French criterion B, "Permanent signs of the illness for at least six months", is very comparable to D in the American definition, although the active phase of the disease can be shorter. In addition, the French B2 is comparable to the American definition B, stressing deterioration of the level of functioning.

The French criterion A1, "Severe disturbance of the train of thought", can be compared with DSM criterion 1.C, "Incoherent or marked loosening of associations". The French A2, "Severe affective disturbance", can be compared with DSM A.1.e, "Flat or grossly inappropriate affect". Hallucinations are not stressed in the French definition, presumably because if prominent they lead to a diagnosis of a chronic hallucinatory psychosis.

Delusions are included among the symptoms of "alteration of the experience of reality", A3, in the French definition, where they occur as an alternative to depersonalisation and derealisation. By contrast, derealisation and depersonalisation are not mentioned in the American definition, and they are not usually regarded as definitely psychotic phenomena in the anglophone countries.

The specific "Bizarre delusions" (A2) and hallucinations commenting on the patient or conversing etc. (A3) mentioned in the DSM, both of which would be regarded as important diagnostic features of schizophrenia by anglophone psychiatrists, do not seem to be given anything like the same importance by the French; who do not seem to consider Schneiderian 'First Rank' symptoms as important diagnostic characteristics of schizophrenia. These 'First Rank' symptoms are of course the theoretical basis of almost all anglophone definitions of schizophrenia, including those in the DSM, the Present State Examination and the CATEGO computer program.

In the French criteria, C requires age of onset of less than 40 years. No age of onset is specified in DSM-III-R.

Both sets of criteria exclude organic factors: the French (E) specifies these as organic states, alcoholism or drug abuse, whereas in the DSM these are all presumably to be included under "organic factors". French criterion D excludes acute delusional psychosis, which of course is less well recognised in the anglophone countries, and is therefore sufficiently excluded in DSM-III-R by the duration criteria. The French criteria, under F, make it possible for a probable diagnosis to be made when the time criteria have not been fulfilled. Both sets of criteria exclude affective states, the DSM-III-R under C and the French criteria under G. There is no specific mention in the French criteria dealing with a history of autism: this is found only in the DSM criteria, at F.

Looking at the DSM subtypes, it would seem possible that the Catatonic, Disorganised, Undifferentiated and Residual types correspond to the French criteria, whereas it is possible that at least some from the Paranoid subtype would merge with the Delusional Paranoid Disorders and meet the French criteria for either Chronic Hallucinatory Psychosis or Chronic Delusional Psychosis.

Thus it would appear probable that the DSM-III-R criteria would encompass a larger group of patients within the concept of Schizophrenia, taking in a few patients whom the French would put into the 'Acute Delusional' group, more from the 'Chronic Delusional' group, and nearly all of the 'Chronic Hallucinatory Psychoses' group.

Chronic Hallucinatory Psychosis

The criteria for the Chronic Hallucinatory Psychosis are as follows.

A. At least three of the following four manifestations for at least one month

A1. *Internal auditory hallucinations.* At least one of the following:
- (a) auditory hallucinations in which one or more voices keep up a continuous commentary on the behaviour or thoughts of the subject
- (b) auditory hallucinations in which one or more voices continuously express the thoughts or reading of the subject or echo them
- (c) auditory hallucinations in which two or more voices converse among themselves.

A2. *Delusional ideas of influence.* At least one of the following:

(a) delusional ideas in which sensations, impulses or actions are experienced as being imposed by an external force
(b) delusional ideas in which thoughts are experienced as being imposed by an external force
(c) delusional ideas in which the subject is convinced that thoughts have been stolen
(d) delusional ideas in which the subject is convinced that others know his thoughts.

A3. *Hallucinations of any type*

A4. *Delusional ideas of any type*

B. Permanent signs of the illness for at least six months, with the permanent presence of at least one of the following.

B1. Presence of any of the manifestations A1, A2, A3 or A4.

B2. Deterioration from the pre-morbid level of professional, domestic or scholastic functioning.

B3. Deterioration from the pre-morbid level of functioning in social relationships.

B4. Social isolation or withdrawal into oneself.

B5. Irrational, illogical, bizarre or magical thinking or thinking with a delusional colouring.

B6. Bizarre or grossly disorganised behaviour.

C. Has never corresponded to the A1 symptoms of the criteria for Chronic Schizophrenia (i.e. "Severe disturbance of the train of thought").

D. Does not correspond to the criteria for an acute delusional psychosis.

E. Organic, alcoholic and drug abuse states are excluded.

F. If the patient has criteria A and B but not for long enough, then the probable diagnosis may be made.

G. Affective states are excluded.

This separate category of Chronic Hallucinatory Psychosis is not met with in the anglophone literature at all. The symptoms in A1 and A2, one of which has to be present for at least one month under the French criteria, correspond closely to Schneiderian First Rank symptoms. Nearly all these cases therefore would probably be included under Schizophrenia rather than under the Delusional (Paranoid) Disorders by anglophones, as these symptoms are regarded as typical of Schizophrenia.

The time criteria and exclusion criteria are much the same in both sets.

In C, where the French exclude cases showing thought disorder, which they appear to regard as the main symptom of Schizophrenia, one can make comparisons with the A.1.c criteria of DSM–III–R, and comment that again these would cause most of these cases immediately to be included within the DSM definition of Schizophrenia.

Recently, Bourgeois & Degeilh (1988) have discussed the continuing French attachment to the concept of Chronic Hallucinatory Psychosis, which has its roots, as does *Bouffée Délirante*, in the theories of degeneration. Certainly it is believed to occur usually in a predisposed personality, and the typical patient is described as ". . . a woman of around 50, presenting acutely a rich hallucinatory syndrome, with a good therapeutic response to neuroleptics and maintaining a certain level of social adaptation" (author's translation). Bourgeois & Degeilh comment that in their experience there is an even better response to antidepressants and especially to electroconvulsive therapy, and they speculate as to whether it is not by nature more of an affective condition. They point out that it is mentioned in all the French psychiatric textbooks (except those published in Canada).

Chronic Interpretative Psychoses

The Chronic Interpretive (or Delusional) Psychoses have the following empirical criteria.

A. Delusional ideas for at least a month, characterised by each of the following.

A1. Their systematisation. Either

(a) delusional ideas organised on a single overwhelming theme; or
(b) delusional ideas organised on a series of obvious themes.

A2. Their theme(s). At least one of the following:

(a) delusions of persecution
(b) delusions of jealousy
(c) delusions of claims and/or injustice (French word is *revendication*)
(d) delusional sexual ideas (possibly de Clérambault's syndrome; the French adjective used is *érotomaniaques*)

A3. Their mechanism. Either

(a) delusional ideas limited to those concerned with interpretation; or
(b) delusional interpretive ideas of primary origin.

(These appear to correspond to the anglophone Primary (b) and Secondary (a) Delusions.)

B. Permanent signs of the illness for at least six months, with the constant presence of B1 or B2.

B1. The uninterrupted presence of delusional ideas responding to the criteria in A.

B2. Both

- (a) the criteria for Paranoid Personality; and
- (b) deterioration since the onset of the illness in social relationships.

C. Has never corresponded to the A1 criterion for Chronic Schizophrenia (i.e. "Severe disturbance of the train of thought").

D. Exclusion of acute delusional psychosis.

E. Exclusion of organic illness, alcoholism or drug abuse.

F. Probable diagnosis may be made when only the time scale is too short.

G. Not due to an affective psychosis.

These criteria for Chronic Interpretive Psychoses are most comparable to the criteria for the DSM grouping Delusional Paranoid Disorder (ICD 297.10). The French stress the systematisation of the delusions, which is a cardinal feature in the developmental history of their system of classification; whereas the Americans stress that the delusions should be non-bizarre. To some degree the French A2 criterion makes the same point by setting out non-bizarre themes.

Under B, the permanency and duration of six months is much the same. The French C stresses that patients must not satisfy the A1 criterion (thought disorder) of Chronic Schizophrenia. Thought disorder in itself would not be such an important point to the anglophone psychiatrist unless it led to odd or bizarre behaviour, which would be excluded under DSM criterion C. In the American definition, Schizophrenia is excluded under E, again by reference to "Schneiderian First Rank" Hallucinations and Delusions; otherwise the exclusions are again much the same.

It is interesting that here the DSM specifications for subcategorisation by type of delusion are very similar to the French; Jealousy, Persecution and Erotomanic being specifically mentioned. The French A2(c) *revendication* is probably very similar in concept to the DSM subtype Grandiose, although the French would perhaps stress that the individual has a claim which is not being recognised. There is no mention in the French system of the somatic type.

Auditory or non-visual hallucinations are allowed under B in the DSM classification; they are not mentioned in the French, so are presumably not definitely excluded. The French classification also stresses the importance of a paranoid pre-morbid personality and deterioration of functioning, whereas this is not stressed in the DSM criteria, except that under C, "Apart from the delusion(s) or its ramifications, behaviour is not obviously odd or bizarre." Deterioration might be taken to warrant exclusion. In anglophone psychiatry the ability of 'paranoid patients' to go on behaving relatively normally, keeping their delusions strictly to themselves, is felt to be the main distinguishing feature if this grouping is to be allowed a separate identity. Deterioration is felt to be the hallmark of a true Schizophrenia.

Acute delusional psychoses

Finally the French classification offers two acute delusional psychoses, those "considered to be Schizophrenic" and those "considered to be Bouffées Délirantes".

The concept of an acute reactive and non-progressive schizophrenia-like psychosis, which remits completely, has been discussed in anglophone psychiatry for many years, without apparently any real consensus being achieved as to whether these cases are simply mild cases of schizophrenia which will eventually show deterioration if the patient survives long enough, or a separate 'third psychotic disorder'.

The five INSERM subcategories are here reduced to two, the Schizophrenic Acute Delusional Psychoses and the Bouffées Délirantes. Both may be either reactive or spontaneous.

Acute Delusional Psychoses Considered to be Schizophrenic

The Acute Delusional Psychoses considered to be Schizophrenic have the following empirical criteria.

A. Delusional ideas of any type.

B. Acute onset in less than a week, or sub-acute in less than four weeks, of delusional ideas.

C. Fulfils criteria A and B for Chronic Schizophrenia except as far as duration is concerned.

D. Age of onset before 40.

E. Does not satisfy the criteria for *Bouffée Délirante*.

F. Not due to an organic, alcoholic or drug-abuse state.

G. Not due to an affective state.

The Schizophrenic Acute Delusional Psychoses can be compared with Schizophreniform Disorder in DSM-III-R – that is, illnesses meeting criteria A and C of DSM Schizophrenia but lasting less than six months – especially if the brief reactive psychoses with prominent emotional turmoil and impaired reality testing (?confusional or oneiroid states) are excluded, as they are under C in the DSM and E in the French system. In the French definition, delusional ideas of any type are allowed, whereas in the American they have to correspond to those specified for Schizophrenia. The period of onset is not mentioned in DSM – presumably it is less than six months – whereas in the French criteria it is specified as being less than a week (acute onset) or less than four weeks (sub-acute onset). Age of onset is not mentioned in the American criteria. The Americans request the specification of "with or without good prognostic features", which are stated, two of them (2 and 4) resembling criteria for *Bouffée Délirante*, B(a) and B(b). It would appear that with the French criteria a good prognosis is assumed under C.

Bouffée Délirante

The French empirical criteria for Bouffée Délirante are the following.

A. Delusional ideas characterised by each of the following.

A1. Sudden onset in less than 48 hours.

A2. A multiplicity of themes and mechanisms to the delusions (polymorphous delusions).

A3. Absence of organisation on any single predominating theme or obvious series of themes.

B. Disturbance of mental functioning without disorientation in time and space, characterised by at least three of the following.

(a) sudden changes from one emotional reaction to another, e.g. anxiety to anger
(b) sudden changes from one abnormal affect to another, e.g. euphoria to depression
(c) sudden changes of psychomotor behaviour, e.g. from agitation to prostration
(d) depersonalisation or derealisation
(e) hallucinations or unusual perceptions of any type.

C. The disappearance of the pathological features in A and B, with a complete return to the pre-morbid state in less than two months.

D. Absence of any previous psychiatric illnesses other than one or more previous attacks of *Bouffée Délirante*.

E. Not due to organic mental disease, alcoholism or drug abuse.

F. Divides it into two clinical forms:

(a) the authentic type described by Mangan, with absence of demonstrable stress preceding its onset; and
(b) the reactive, with demonstrable preceding stresses

This can be compared with 298.8 Brief Reactive Psychosis in DSM-III-R, which recognises only a reactive form of this condition. The speed of onset is not specified in DSM. DSM criterion B, Emotional Turmoil, mentions rapid change from one affect to another, but the French multiple and rapidly changing delusional ideas are not stressed in the DSM criteria. Under the French criterion C, the state is allowed to last for two months, as compared with one month in the DSM under E. The exclusions are much the same.

Conclusion

It would appear that although there are undoubtedly minor differences, the two systems of classification are converging. This is to be expected, as presumably both systems are classifying the same set of psychiatric illnesses on a clinical basis and trying to group much the same case material into understandable and predictable syndromes.

Certainly the provision of these empirical operational criteria for the French diagnostic groups should, if they gain general acceptance, make it much easier for other psychiatrists to understand the French literature.

Possibly the concept of *Bouffée Délirante* or Brief Non-Reactive Psychosis will eventually gain acceptance in Anglo-American psychiatry. It might also prove possible to merge the French Chronic Delusional Psychoses with the chronic and non-deteriorating Delusional (Paranoid) Disorder of DSM-III-R, the use of which as a separate diagnosis is increasing. The acceptance of Chronic Hallucinatory States as separate from Schizophrenia would, however, seem much less likely in anglophone psychiatry, due to the overwhelming influence of the Schneiderian First Rank symptoms.

References

American Psychiatric Association (1987) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn, revised). Washington DC: APA.

Bourgeois M. & Degeilh, B. (1988) Défense et illustration des psychoses hallucinatoires chroniques. *Annales Médico-Psychologiques*, 146, 490–502.

Institut National de la Santé et de la Recherche Médicale, Section Psychiatrie (1969) Classification française des troubles mentaux. *Bulletin de l'Institut National de la Santé et de la Recherche Médicale*, 24, Suppl. to No. 2.

PELICIER, Y. (1976) *Lexique/Psychiatrie*. Paris: Presses Universitaires de France.

PICHOT, P. (1982) The diagnosis and classification of mental disorders in French-speaking countries: background, current views and comparison with other nomenclatures. *Psychological Medicine*, 12, 475–492.

PULL, M. C., PULL, C. B. & PICHOT, P. (1987*a*) Des critères empiriques français pour les psychoses – II. Consensus des psychiatres français et definitions provisoires. *L'Encéphale*, **XIII**, 53–57.

——, —— & —— (1987*b*) Des critères empiriques français pour les psychoses – III. Algorithmes et arbre de décision. *L'Encéphale*, **XIII**, 59–66.

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The Delineation of Schizophrenia from other Psychiatric Illnesses

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Evidence is provided in support of the nosological concept which distinguishes schizophrenia from borderline states. Differentiation of these disorders by a computer pattern-recognition program was based on the initial descriptive characteristics of patients. As a result, we observed good correlation between computer diagnosis from data on 215 patients and follow-up data analysed according to the criteria of Kraepelin's model of schizophrenia and its course. According to the findings on outcome, the states designated as 'sluggish schizophrenia' (or 'slowly developing variant of schizophrenia') comprise a group of dissimilar psychiatric disorders, including borderline states and cases of process schizophrenia, with the specific initial symptoms of the latter disease.

According to the nosological concept of Kraepelin (1904), analysis of the presenting clinical picture of psychiatric illnesses and disturbances permits the identification of cases of dementia praecox (DP or schizophrenia). This diagnosis implies an accurate prognosis for the most important characteristics of the course of the disease. According to Kraepelin's (1904) data, and depending on the form of the illness, an unfavourable outcome, with the development of a specific psychological defect, is responsible for social and vocational decline in 90–100% of cases of the disease. Kraepelin also described variants of the remission periods of the disease including, for instance, the so-called 'transient recovery' which was then followed, at times after decades, by psychotic episodes characteristic of DP, and ultimately a typical psychiatric defect.

The principal difficulty in confirming Kraepelin's concept was that it allowed a broad pattern of presentation for the disease. Admitting broad criteria for the symptoms of the illness, beyond the limits of the basic model, leads to a loss of specificity: the diagnosis of DP becomes blurred, does not help with prognosis, and makes it impossible to predict the long-term course of the disorder.

It should be remembered that at the initial stages of the development of his theory, Kraepelin himself (1904) put forward the idea of atypical, attenuated, non-psychotic forms of DP. Later this idea was embodied within rigorous, well defined, narrow boundaries. However, Bleuler (1911) developed a broad concept of 'dementia praecox'/'schizophrenia'. He described 'simple' and 'latent' forms of schizophrenia, to which he attributed many syndromes or clinical presentations with 'borderline' symptoms, e.g. personality disorders, neuroses, alcoholism, and which, in his view, progressed without serious social or vocational disturbance. He emphasised that the 'schizophrenic' nature of these disorders was confirmed by the fact that these patients previously exhibited "mild pathological symptoms which in the light of a new illness should undoubtedly be considered schizophrenic" (Bleuler, 1911, p. 196). However, many of Bleuler's mild schizophrenic symptoms were ill-defined, and were open to different interpretations.

The fact, for instance, that the patient chooses the same path during walks was considered to be a sign of "autism" (Bleuler, 1911, p. 53). Bleuler's interpretation of "negativism", a schizophrenic symptom, was unjustifiably broad and vague, as Kraepelin (1913) pointed out. So were Bleuler's definitions of emotional changes and some other symptoms. Bleuler also gave too broad a definition of "schizophrenic dementia", which included non-pathological traits characteristic of gifted people, namely their ability to integrate all intellectual associations in one complex, a "tendency towards the new, an unusual train of thoughts, and deviation from traditions" (Bleuler, 1911, pp. 73–74). Kraepelin (1913) later emphasised the danger of excessive diagnosis of DP, in the context of discussion of Bleuler's views on schizophrenia.

The concept of 'simple' and 'latent' schizophrenia and their different variants did not gain wide acceptance, and was subjected to sharp criticism (Wirsh, 1960; Parkin, 1966; Weisfogel *et al*, 1969).

It has also been suggested that the concept of 'latent' schizophrenia expanded the boundaries of the disease so much that they completely disappeared.

Until recently, psychiatric practice in Great Britain was dominated by Kraepelin's diagnostic approach to schizophrenia (Clare, 1976). In identifying this disease, psychotic symptoms were primarily analysed with regard to the specific changes in the personality. Special emphasis was put on revealing the 'first-rank' symptoms (Schneider, 1962; Mellor, 1970; Wing *et al*, 1972). In diagnosis, much consideration was given to revealing the so-called 'primary delusion' (Jaspers, Gruhle), and typical catatonic symptoms (Kraepelin, 1904; Mayer-Gross *et al*, 1954). British textbooks of psychiatry did not aim to single out Bleuler's 'latent' schizophrenia or its analogues, 'pseudoneurotic' and 'pseudopsychopathic' forms of schizophrenia (Mayer-Gross *et al*, 1954; Merskey & Tonge, 1974; Tredgold & Wolff, 1979). At the same time, British psychiatrists did not rule out the possibility of 'pseudoneurotic syndromes' in the initial stages of the disease, nor the occurrence of a progressive course unfolding slowly at first. The simple form was often regarded as a variant of schizophrenia terminating unfavourably.

A distinction is clearly drawn between schizophrenia and borderline states in ICD-9 (World Health Organization, 1978), which does not recommend that any cases of schizophrenia be diagnosed as 'latent', 'pseudoneurotic', or 'pseudopsychopathic'. The approach taken in the USA in the classification of psychiatric illnesses is essentially the same (American Psychiatric Association, 1980).

However, attempts continue to be made to question Kraepelin's requirement that schizophrenia be definitely distinguished from other psychiatric illnesses, including borderline states. According to Hays (1984), for instance, schizophrenia should not be considered by DSM-III to be a separate nosological category. Such an approach obscures the problem of differential diagnosis of this disease. Snezhnevsky *et al* (1983) sought to revive what was known as 'latent' schizophrenia by advancing the concept of 'sluggish' or 'slowly progressive' schizophrenia.

Further efforts are obviously needed to confirm the thesis that schizophrenia constitutes a separate clinical entity distinguishable from the so-called borderline states. This thesis does not permit an extension of boundaries of schizophrenia by classifying the so-called 'latent' or 'slowly progressive' variants within this disease, and refutes the insistent claim that they are intermediate forms of illness between schizophrenia and borderline states.

The fact that schizophrenia has a clear-cut boundary has been confirmed by a study in which 312 patients were analysed using 85 descriptors, and a computer diagnosis made (Kazanetz, 1979). Pattern-learning and pattern-recognition programs for the purposes of differential diagnosis are capable of using the patients' characteristics recorded during the first psychotic episode. Such differential diagnoses correlate well with clinical diagnoses that take into account the specific features of the subsequent course of the disease (Kazanetz, 1979).

The previous study investigated the distinction between patients with exogenous psychiatric illness and patients with schizophrenia in whom exogenous factors were recorded as precipitants for the psychotic episode. In this study the possibilities were explored for nosological differentiation of patients who on first admission showed symptoms of hypochondriasis, dysmorphophobia, anxiety, fear, depression, etc. Such symptoms, when observed early in the course of illness, distinguish schizophrenia from the borderline states.

This study was conducted in the following sequence. Patients were selected if they presented with symptoms which raised the question of the differential diagnosis of schizophrenia or borderline disorders. A computer diagnosis was then made for these patients; the program applied was capable of distinguishing schizophrenia from the borderline states, according to the diagnostic criteria of Kraepelin's model. These initial computer diagnoses were compared with final computer diagnoses based upon follow-up data. In this way the hypothesis was tested that schizophrenia is definitely distinguishable from the borderline states.

Method

Patient selection

All admissions to the Gannushkin Hospital in Moscow from a specific catchment area were reviewed. Patients were selected if the record of the first admission indicated self-referential ideas (see footnote). In such ideas of self-reference the subject is the patient himself. Otherwise, passivity experiences may be referred to (Zaitsev, 1972). The symptoms sought were hypochondriacal or dysmorphophobic ideas, including those accompanied by anxiety and fear, depression with ideas of guilt or worthlessness etc., ideas of reference or influence and other passivity experiences, including delusional experiences and delusional-like ideation, overvalued ideas, and monosymptomatic preoccupations or delusions.

A total of 255 such patients were selected for further examination out of 700 records, all of them aged 16–40 at the time of first admission. Patients were selected who had been diagnosed as having schizophrenia (including 'slowly progressive' schizophrenia) or as having a borderline status, affective psychoses, etc. (ICD-9: 300, 301, 310, 296, 298, etc.). Patients initially diagnosed with alcoholic psychosis were excluded.

Most of those selected could be followed up for 20 years. Sometimes the follow-up period had to be shorter (e.g., when some patients originally supposed to have slowly progressive schizophrenia died of a somatic disease).

Record sheet for computer diagnosis

A new version of the record sheet (see below) contained 27 descriptors used to provide descriptive clinical information about each patient. Each descriptor was assigned a value, positive or negative, to indicate whether or not the symptoms involved were found in the initial case history. The items in the record sheet were completed using information culled from the narratives in the charts. The characteristics employed as descriptors could have only a presumptive, complex relationship to the main diagnostic features of the disorders to be differentiated. A descriptor is marked for coding by 1 or 0 according to whether or not the characteristic involved is observed. Program processing of the record-sheet data enabled the relevant diagnostic information to be extracted and represented integrally as a unique diagnostic solution.

Record sheet

Patient name
First admitted
Discharged
(1) Purposeless motor agitation
(2) Motor excitement, aimlessness, with profound cognitive and behavioural disorganisation
(3) Affective excitement, diffuse but retaining a distinct affective quality, i.e., fear or terror during hallucinations, extreme melancholic agitation, etc.
(4) Impulsive acts, including aggression
(5) Inappropriate or incongruent motor acts (grimaces, fanciful motions, affectedness, stereotyped behaviour, echolalia, gross giddiness, etc.)
(6) Degrees of catatonic stupor
(7) Other types of stupor
(8) Degree of orientation in the case of catatonic stupor
(9) Self-referential ideas*, excluding ideas of grandeur: hypochondriac ideas, ideas of guilt, worthlessness, dysmorphophobic ideas, etc.
(10) Self-referential interpretations of sensation, producing ideas like those in item 9, comprising ideas which arise on the basis of paraesthesias, unpleasant physical sensations, or painful somatic sensations
(11) Self-referential interpretations producing ideas as in item 9, associated with depersonalisation, derealisation or dysmorphophobic effects
(12) Self-referential ideas arising from an altered process of thought
(13) Self-referential ideas linked to particular themes and associated set attitudes
(14) Self-referential ideas secondary to affective states such as depression or fear
(15) Self-referential ideas associated with hallucinations, ideas of influence, persecution, etc.
(16) Self-referential ideas not associated with the above-mentioned factors, unrelated to the effects listed under items 10–15
(17) Predominant affect of elation
(18) Predominant affect of dysphoria (irritability, captiousness, demanding behaviour)
(19) Withdrawal, refusal to talk, reticence, distrust
(20) Self-referential ideas which are potentially appropriate, such as an attempt to convince the physician that the origin of the complaints is well grounded, associated with a request for treatment (without thought disorder)
(21) Self-referential ideas of an 'altruistic' type, expressing concern that the patient might be guilty of harming people or being guilty in the eyes of society
(22) Bizarre content in self-referential ideas
(23) Complaints reflecting passivity experiences, thematically linked with self-referential ideas
(24) Self-referential ideas secondary to passivity experiences in the absence of any actions of those around the patient
(25) Disorganisation of thought or ideas, concomitant with the expression of self-referential ideas (the patient does not know where he is or considers that he is in another place; the patient is subject to specific features of hallucinations or delusions)
(26) Thought insertion, broadcasting of thoughts, thought withdrawal, audible thoughts
(27) Subjective inhibition of thinking presenting as difficulty of concentration and in the performance of mental functions.

Diagnostic characteristics of the program

Schizophrenia was delineated from non-schizophrenic disorders with the use of the Kora–3 pattern-learning and pattern-recognition program discussed elsewhere (Kazanetz, 1971, 1979). The Kora–3 program is capable of taking information from the psychiatric history and follow-up, and using it to develop a method of diagnosis of psychiatric syndromes. A different approach to computer diagnosis of psychiatric illnesses and schizophrenia dealt with the problem of simulating the decision-tree of the clinician, while making a diagnostic interpretation of the results of the psychiatric interview (Overall & Hollister, 1979; Freedman *et al*, 1980).

The Kora–3 program has two phases: learning and examination. In the learning phase, 20 patients rediagnosed on follow-up with schizophrenia were used together with 20 who were rediagnosed as having non-schizophrenic disorders. Kraepelin's model of the course of schizophrenia was taken as the standard in confirming the diagnosis. In the learning phase, the program used data on verified diagnoses to generate the rules for delineation of schizophrenia from non-schizophrenic disorders. Such rules of differential diagnosis were formed by singling out sets of recognition triads – combinations of patients' initial characteristics taken three at a time. Thus some of the recognition triads were taken to indicate schizophrenia, and the others non-schizophrenic disorders.

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*Note: the expression "self-referential ideas" occurs repeatedly here. The significance of this phrase from Zaitsev in some Russian psychiatric practice is to denote certain ideas in which the patient feels that he/she suffers from an action or influence of an external agent. Alternatively, in reporting such an experience the patient refers to himself as a subject. These experiences are considered by the examiner to arise from within the patient, but are interpreted secondarily by the patient as being due to another agent operating inside the individual, e.g., another voice speaking the patient's thoughts. This is different from so-called extroverted ideas, such as other passivity feelings, in which a purely external effect is reported, e.g. from hypnosis or rays operating from a distance. There is no simple translation of this expression which may seem redundant to the English-speaking practitioner.

The remaining 215 patients who had not been entered in the learning phase were given a diagnosis by computer during the examination phase. The computer used only the initial descriptive data coded on the record sheets. The recognition triads formulated during the learning phase served as the basis for the computer diagnosis of the initial state of all 255 patients. When the triads indicating schizophrenia predominated, the patients were diagnosed with schizophrenia: otherwise the computer diagnosis was of non-schizophrenic disorder.

Verification of the computer diagnosis

The criteria used to verify the computer diagnoses of schizophrenia were in accordance with Kraepelin's model of the course of the disease, but modified to take into account the effects of comprehensive treatment for schizophrenia. Kraepelin's model involves two principal features. One of them is the propensity to develop chronic changes which include characteristic affective disorders, typical formal thought disorders, paralogical thought, thought blocking progressing to disorganisation of thinking, and a tendency to create neologisms, etc. Kraepelin's other principal feature of schizophrenia is its tendency to spontaneous exacerbations with typical psychotic symptoms, e.g., negativism, impulsivity, bizarre and repetitive mannerisms and stereotypies, states of catatonic motor excitation, and stupor, without severe disorientation (Kraepelin, 1904), 'primary delusional process', etc.

The diagnosis of schizophrenia can be considered on the basis of follow-up in the case of a severe schizophrenic defect with social or vocational decline or both. This is designated by Kraepelin (1904) as a 'severe' or 'moderate' degree of dementia.

For patients with mild changes in mental state, the computer diagnosis of schizophrenia is confirmed by acute exacerbations with typical psychotic symptoms, e.g. catatonic disturbance, primary delusions, etc. These spontaneous exacerbations of psychosis testify to the schizophrenic nature of even relatively mild changes in the persona, such as withdrawal, a limited range of interests, and loss of facility in social adaptation.

As a whole, Kraepelin's model of the course of schizophrenia has rather distinct features, and can easily be demarcated from all possible dynamic changes or variations of course due to non-schizophrenic disturbances, especially borderline states.

TABLE I

Follow-up data on patients diagnosed by computer

Computer diagnosis	*Total no. of cases*	*Number of cases confirmed at follow-up*
Schizophrenia	92	92
Non-schizophrenic disorders	123	116
Total	215	208

Results

Results of rediagnosis

Of the 215 patients from the examination phase, 92 were diagnosed by computer as having schizophrenia, and 123 as having non-schizophrenic disorders, mostly borderline states (neuroses, personality disorders, non-psychotic disorders due to structural brain lesions, various somatic illnesses, etc.). Table 1 summarises the comparison between the computer diagnosis and the findings on follow-up.

Verification at follow-up of the initial computer diagnoses

Schizophrenia

For all 92 patients diagnosed as schizophrenic by the computer initially, the diagnosis was identical on computer analysis at follow-up. For 72 of these patients, a chronic social decline and loss of ability to work or advance professionally was accompanied by marked changes characteristic of schizophrenia: autism, apathy, emotional hypoaesthesia, inappropriate emotional responses, severe poverty of thought, paralogia, neologisms, disordered behaviour, etc. The exacerbations of the psychosis occurred spontaneously during the period of observation in all the patients with prominent schizophrenic defect.

Some of the patients rediagnosed by the computer as schizophrenic retained adequate social and vocational adaptation throughout the follow-up (20 patients) (Table II). During lengthy remissions (7–19 years for 16 patients), these patients underwent relatively little change in their mental status, with withdrawal, impoverishment of emotional life, and sometimes pseudopsychopathic disorders or paranoid mood. The schizophrenic nature of the illness in these patients with a mild course was confirmed by the record of acute spontaneous exacerbations with psychotic symptoms. In the context of one or another of these episodes, 15 patients had ideas of hypnotic or other unusual influence, thought insertion, thought broadcasting, delusional states with hallucinatory voices, and 'mental conversations'. Five patients suffered catatonic symptoms.

Twenty-five patients diagnosed with schizophrenia by the computer had an initial diagnosis, made by the physician in charge, of 'sluggish schizophrenia'. Judging from the subsequent unfavourable course of the schizophrenic

TABLE II
Relapse and deterioration in confirmed cases

Computer diagnosis	*Cases confirmed at follow-up*	
	Repeated hospital admissions	*Social and vocational decline*
Schizophrenia	90	72
Non-schizophrenic disorders	44	13
Total	134	85

process, to diagnose these patients as 'sluggish' schizophrenics was an undeniable mistake.

Non-schizophrenia disorder

Of the group 'examined' by the computer, 123 patients were diagnosed as having non-schizophrenic disorders. The diagnosis was verified on follow-up in 116 (94%). During the first computer diagnosis the initial conditions of the patients suffering from non-schizophrenic disorders were classified as follows in accordance with the ICD–9 nomenclature:

neurotic disorders (coded 300)	28 patients
psychopathy (coded 301)	23 patients
non-psychotic disorders due to structural brain lesions, various somatic disturbances (coded 310 etc.)	37 patients
psychoses arising from transient organic diseases (coded 293)	7 patients
affective psychoses (coded 296)	10 patients
reactive (non-organic) psychoses (coded 298)	11 patients

The great majority of patients (103 out of 116) whose computer diagnoses were confirmed as non-schizophrenic showed good social and vocational adaptation: they regained their jobs and often advanced professionally (Table II). They recovered quite well both intellectually and emotionally; at the same time, many patients complained of headaches, unusual fatigue and irritability.

The patients this group were often erroneously diagnosed as having a schizophrenic defect by the physicians in charge. Transient asthenic and affective disorders were taken to be schizophrenic defect, and were identified by the physicians with emotional hypoaesthesia, emotional inadequacy, autism, etc. That such diagnostic decisions had been wrong would become clear in the light of the subsequent follow-up data on the patients involved.

In 13 patients diagnosed by the computer as having non-schizophrenic disorders, social and vocational adaptation was found to have deteriorated steadily during the follow-up period. Decompensation of this kind was usually complicated by alcoholism, somatic disease, or acute state organic process in the brain. The characteristic changes in the mental status of these patients were pronounced asthenia, increased emotional lability, hypochondriacal concerns, and personality changes of an organic nature (ICD–9 310.0–2, 310.8, etc.).

For 44 of the patients diagnosed by the computer and verified as being non-schizophrenic, deterioration of mental state and repeated hospital admissions were recorded at least once during follow-up. Such deterioration was ordinarily preceded by some exogenous hazards (psychic trauma, somatic disease, alcoholic excess, etc.). In three patients, the late worsening of the mental state could be attributed to the specific features of the progression of affective psychosis (recurrent period of depression).

In nine patients of verified borderline state, the patients were repeatedly readmitted throughout follow-up (except the patients with concomitant alcoholism or drug addiction). In all these cases of frequent episodes of deterioration of the mental state with repeated admissions, the patients retained the ability to work well professionally, and social adaptation was not affected up to the end of the follow-up period.

The above-mentioned changes observed at the later stages of the follow-up period can hardly be regarded as being due only to previous adverse life events. The life events revealed in the follow-up study of these patients were often less severe than for other patients with an identical initial diagnosis, who suffered no unfavourable effects. The group of patients under discussion may be considered predisposed to an abnormal response to stressful life events.

This study was concerned with the symptoms typical of non-schizophrenic patients displayed during the periods of deteriorated mental states – symptoms of affective instability (such as depression, anxiety, fear), an asthenic syndrome, cenesthesopathic (hypochondriac) states, delirious pictures. During the follow-up period these patients often exhibited secondary delusional-like disorders (diffuse ideas of reference), developed within the framework of depression, grief reactions, etc. No psychotic symptoms typical of schizophrenia were noted in this group of patients (no first-rank symptoms, 'primary delusion' effects, catatonic symptoms specific to schizophrenia).

Of the 102 patients diagnosed as non-schizophrenic by the computer and diagnosed as schizophrenic by their clinicians, 84 had received a diagnosis of 'sluggish' schizophrenia.

Discussion

The argument has been tested that the features specific to the first episode of schizophrenia make this disease distinguishable from the other mental disorders and borderline states in particular. Symptoms for differential diagnosis were identified during the learning phase of the Kora–3 program.

The results of computer diagnosis correlated well with the follow-up data. The computer diagnosis was not verified on follow-up in 3% of cases; the total number of non-verifications can reach 9% if there are errors in the computer diagnosis due to the difficulty in identifying certain descriptors, for instance those dealing with the degree of the patient's disorientation (stages of level of consciousness). If states of disorientation occur, the diagnostic meaning of many descriptors changes markedly. So the symptoms specific to schizophrenia are within definite limits and consistent during the subsequent course of the illness.

There is no reason to subdivide verified cases of schizophrenia into rapidly developing and 'sluggish' forms. According to the follow-up data, most cases of schizophrenia originally classified by the physicians as 'sluggish' later proved to be manifestly typical cases of schizophrenia with prominent deterioration. Those variants of schizophrenia that were classified as borderline states by the initial computer diagnosis cannot be considered atypical, 'sluggish' schizophrenia, as the deterioration of such patients was later found to be typical of 'process' schizophrenia. Thus the situation is indicative of an erroneous initial diagnosis (due perhaps to a lack of attention to some phenomenological characteristics).

Patients initially diagnosed as non-schizophrenic who later had repeated deterioration of their mental state do not have only one clinical pattern. We have to presume that these patients have a predisposition to relapse, and it would not be justified to classify such patients as schizophrenic. One should take into account the fact that the course of the disorder is generally favourable, and that during the periods of relapse the patients do not show the symptoms characteristic of schizophrenia.

In summary it may be concluded that the argument is unfounded that the symptoms of schizophrenia are broad and non-specific, and connected with those of borderline states.

References

AMERICAN PSYCHIATRIC ASSOCIATION (1980) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn) (DSM-III). Washington, DC: APA.

BLEULER, E. (1911) *Dementia praecox oder Gruppe der Schizophrenien*. Leipzig-Wien: Deuticke.

CLARE, A. (1976) *Psychiatry in Dissent*. London: Tavistock Publications.

FREEDMAN, M., KAPLAN, H. I. & SADOCK, B. J. (1980) *Modern Synopsis of Comprehensive Textbook of Psychiatry* (2nd edn). Baltimore: Williams and Wilkins Co.

HAYS, P. (1984) The nosological status of schizophrenia. *Lancet i*, 1342–1345.

KAZANETZ, E. PH. (1971) *Principles of Diagnostic Control in Psychiatry on the Basis of the Computer*. Thesis (in Russian), Moscow.

—— (1979) Differentiating exogenous psychiatric illness from schizophrenia. *Archives of General Psychiatry*, 36, 740–745.

KRAEPELIN, E. (1904) *Psychiatrie*. 7 Aufl., 2 Band. Leipzig: Verl. von Barth.

—— (1913) *Psychiatrie*. 8 Aufl., 3 Band. Leipzig: Verl. von Barth.

MAYER-GROSS, W., SLATER, E. & ROTH, M. (1954) *Clinical Psychiatry*. London: Cassel.

MELLOR, C. S. (1970) First rank symptoms of schizophrenia. *British Journal of Psychiatry*, 117, 15–23.

MERSKEY, H. & TONGE, W. L. (1974) *Psychiatric Illness* (2nd edn). London: Baillière Tindall.

OVERALL, J. E. & HOLLISTER, L. E. (1979) Comparative evaluation of research diagnostic criteria for schizophrenia. *Archives of General Psychiatry*, 36, 1198–1205.

PARKIN, A. (1966) Neurosis and schizophrenia. II. Modern perspectives. *Psychiatric Quarterly*, 40, 217–235.

SCHNEIDER, K. (1962) *Klinische Psychopathologie*. 6 Aufl. Stuttgart: Georg Thieme Verlag.

SNEZHNEVSKY, A. V. (ed.) (1983) *Psychiatry Handbook in Two Volumes*, vol. 1 (in Russian). Moscow: Medicina.

TREDGOLD, R. F. & WOLFF, H. H. (1979) *U.C.H. Handbook of Psychiatry*. London: Duckworth.

WEISFOGEL, J., DICKES, R. & SIMONS, R. C. (1969) Diagnostic concepts concerning patients demonstrating both psychotic and neurotic symptoms. *Psychiatric Quarterly*, 43, 85–122.

WING, J. K., COOPER, J. E. & SARTORIUS, N. (1972) *The Measurement and Classification of Psychiatric Symptoms*. London: Cambridge University Press.

WIRSCH, J. (1960) In *Klinische Psychiatrie*, pp. 1–27. Berlin, Gottingen, Heidelberg: Springer-Verlag.

WORLD HEALTH ORGANIZATION (1978) *Mental Disorders: Glossary and Guide to their Classification in Accordance with the Ninth Revision of the International Classification of Diseases* (ICD-9). Geneva: WHO.

ZAITSEV, S. G. (1972) In *Mathematical Methods in Psychiatry and Neurology* (eds Tonkonogy & Jovlev) (in Russian), pp. 94–96. Leningrad: RSFSR Ministry of Health, V. M. Bekhterev Psychoneurological Research Institute of Leningrad.

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Slowly Progressive Schizophrenia – Myth or Clinical Reality?*

A. B. SMULEVITCH

Notes on the translation and editing

We have attempted to render this article into intelligible English. The original was generally somewhat cumbersome. On occasion, a more polished translation might have been attempted, but as the reader should be able to estimate the author's intent, we have avoided any possible liberties in interpretation.

One of us (BZ) worked previously in Moscow, and is familiar with the concepts of the Snezhnevsky school. It is desirable to make some comments, initially, about the general ideas of that school, so as to make the following article more understandable to the Western reader. In brief, the idea of slowly progressive schizophrenia relies on the notion that the individual suffers from a disease which at times presents only minimal symptoms or signs, if any. However, the disease is held to be a nosological entity because thorough and intensive examination will disclose not only the minor signs of psychopathology, but also consistent elements in the family history and changes in the pattern of symptoms from time to time. It is claimed that diagnosis is validated by the long-term outcome.

In examining patients with schizophrenia, the Moscow school often relies upon ideas from the continental European and English literature which are quite familiar in the West. On occasion, neglected notions from the West have been sustained, such as that of the Schub (Mauz, 1930), in which a brief psychotic episode was thought to be followed by a shift in the level of long-term functioning. Some concepts appear to be specific to the Moscow school, for example the reference by Smulevitch in his list of items to a notion which we have translated as "autopsychic residual depersonalisation". This refers to a form of depersonalisation, different from that found in neurotic patients, stationary for the most part, and indicative of a chronic psychosis.

Perhaps the most important idiosyncratic term on which we should comment is the one which we have rendered as 'indistinct forms'. This term has to do with the concept just noted of schizophrenia as a spectrum disease of genetic origin in which the phenotype only partly reflects the genotype, but the diagnosis is confirmed by minute attention to symptoms and phenomenology and their patterns of change over time, as well as the family history. The Russian word means literally 'nearly erased' which could have been translated as 'poorly expressed'. This gives the sense of something which is present but difficult to observe, and which we think is fairly rendered by 'indistinct'.

We have indicated some difficult items by means of comments in square brackets.

One point of meaning which also requires attention has to do with the word 'psychopathic'. In the present context, it is mostly used to mean severe personality disorders. Personality disorders as such are not recognised in the USSR, but extreme versions of neurotic states are often called 'psychopathic'. The word 'psychopathic' should be understood here in that light.

B. Shafran
H. Merskey
B. Zoubok
(for addresses see p. 177)

Reference

Mauz, F. (1930) *Die Prognostik der Endogenen Psychosen*. Leipzig: Georg Thieme.

An article by Merskey & Shafran, entitled 'Political hazards in the diagnosis of slowly progressive schizophrenia', was published in the March 1986 issue of the *British Journal of Psychiatry*. The tendentious direction of this article, aimed at replacing the scientific aspects of the problem with political ones, is clear from the title of this article. The bottom line of the article is not new at all – it implied that the Soviet doctors use psychiatry as a way to fight dissidents and claim that healthy people are psychiatrically ill. The authors try to show that their accusations are not without proof; with this in

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*This is a translation by B. Shafran & B. Zoubok of a paper appearing in 1987 in the *Korsakoff Journal of Neuropathology and Psychiatry*, 87, 1866–1871. It has been edited with notes by B. Shafran, H. Merskey & B. Zoubok, who respond to this article in the following paper in this issue (pp. 174–177).

A request was sent to the Editor of the *Korsakoff Journal of Neuropathology and Psychiatry* for permission to publish a translated version of this paper, but no reply was received.

mind, they try to make the discussion scientific and to show the roots of the 'evil' Soviet psychiatry. The main thought of the article can be summarised as follows: Soviet psychiatrists – some on purpose and others by being misled – are prone to widen the diagnostic framework of schizophrenia, using the term 'slowly progressive schizophrenia'.

Trying to sound scientific, the authors undertake a sort of critical review of the articles published in the *Korsakoff Journal of Neuropathology and Psychiatry* from 1980 to 1984, discussing the different aspects of the clinical picture, social adaptation, and therapy of slowly progressive schizophrenia. The articles discussed were published by the staff of the different psychiatric establishments. Most of them were from the All-Union Research Centre for Mental Health of the Ministry of Health of the USSR, where the problem of slowly progressive schizophrenia has been intensively studied during the last decade. As for the discussion of the specific critical comments by Merskey and Shafran, it is important to stress that they were made in the most unfriendly tone, which is not used in scientific discussion. We must note, for the sake of fairness, that some of their comments are not unfounded. We are talking about some articles with shortcomings in scholarly respects, such as inaccurate quotations from the Western literature and presentation of factual material without data processing by modern statistical methods. Yet on detailed examination of the article by Merskey and Shafran, one can see that these comments do not comprise the true essence of the paper. The authors think that the methodological weaknesses of Soviet psychiatrists make it easier to establish their hidden desire to prove, by any means, the common features of normal states and psychoses (in the understanding of Merskey and Shafran).

The rest of this article is an attempt to prove this point. Merskey and Shafran cannot maintain even the appearance of scientific impartiality, and they allow themselves a very liberal and biased interpretation of the information presented in the Soviet psychiatric publications. They ascribe political meaning to the purely clinical facts published in the *Korsakoff Journal of Neuropathology and Psychiatry*.

Merskey and Shafran comment on the "loss of the sense of distance" [impaired social judgement] which was described as a negative change [like schizophrenic defect]. They not only doubt the possibility of the pathological origin of this disorder, but they further strive to emphasise that such interpretation is made for purely political reasons. They assume that political motivation leads Soviet psychiatrists to place those with "conspicuous lack of respect towards those high in the official hierarchy" among the patients suffering from slowly progressive schizophrenia. Being in doubt about the correct diagnosis of slowly progressive schizophrenia in patients with the manifestations of chronic hypomania, who themselves have asked for specialised help, either in ambulatory settings or in psychoneurological sanatoria, Merskey and Shafran start "defending" these patients. "The presence of such subtle and debatable symptoms," write Merskey and Shafran [in the sense of their nosological nature – AS], "could not justify mandatory hospitalization in the West" (?!).

In allowing or dismissing the diagnosis of slowly progressive schizophrenia, however, it does not make sense to discuss particular questions such as the adequacy of one or another method of presentation of the clinical material or the reliability of identifying some individual manifestations as important.

Let us turn to the matters which in our view are of principal significance. The following thoughts of Merskey and Shafran are worth noticing.

According to their article, slowly progressive schizophrenia has been invented by Soviet psychiatry, by A. B. Snezhnevsky and his school in particular, just for the purpose of turning dissidents into psychiatric patients.

According to Merskey and Shafran, this variety of the course of the endogenous process which is distinguished in the Snezhnevsky classification of schizophrenias as an independent form, does not have its analogues in Western psychiatric classifications (Merskey and Shafran think that the model of pseudoneurotic schizophrenia is out of date and is not used any more). Although the diagnoses of simple schizophrenia and residual defect states are used in the West, these concepts are not clinically comparable to slowly progressive schizophrenia, and they define a narrower spectrum of the disease.

Merskey and Shafran state that the concept of "slowly progressive schizophrenia" in Soviet psychiatry includes, on the one hand, a wide range of psychopathological manifestations which are diagnosed in the West outside the framework of an endogenous process. On the other hand, healthy people are diagnosed with slowly progressive schizophrenia (by mistake or deliberate labelling of healthy individuals as ill).

It is necessary to stress immediately that it is impossible to agree with any of these statements published in the leading English psychiatric journal. But in order that the reader may form his own opinion on the true state of affairs, and to separate the approach determined by clinical reality from the wrong and often perverted interpretation of facts, we will briefly discuss the modern state of the problem of slowly progressive schizophrenia.

First of all, let us note that the concept of slowly progressive schizophrenia is meant for the clinical interpretation of pathological manifestations characteristic of a large contingent of patients which exists, irrespective of the place allocated to it in different modern classifications, or of the political convictions of the medical profession. Significant difficulties in separating this area of psychiatric pathology from symptomatic schizophrenia on the one hand, and borderline states on the other, generate discussion about very general problems such as questions of disease and health, as well as about specific issues of the differential diagnosis, prognosis, and treatment which relate directly to the everyday activity of the psychiatrist.

The problem of slowly progressive schizophrenia is one of the most difficult in modern psychiatry. The difficulties of examining this problem within the framework of general psychopathology are comparable with the difficulties of analysing the so-called 'transitional states' (to which slowly progressive schizophrenia belongs) existing side by side with well-defined clinical forms. [The concept of transitional states reflects a notion of schizophrenia as a disorder spreading along a continuum and related at one end to seemingly neurotic states.] The definition of such kinds of transitional forms in any area of pathology, not only in psychiatry, requires criteria which take into consideration those changes in significant features which show how abnormal behaviour [resembling a personality disorder] reflects the emergence of typical patterns of the illness [e.g. schizophrenic defect, or the description shown in item II.6 of Dr Smulevitch's classification below].

As one of the forms of the well defined nosological class of schizophrenia, slowly progressive schizophrenia represents a separate form of illness, and should not be considered to be an initial (prodromal) phase of symptomatic schizophrenic psychosis. Slowly progressive schizophrenia has a characteristic pattern of development reflecting the dynamics of the endogenous process. It develops slowly over many years, with subclinical manifestations in the latent period, conspicuous symptoms and a subsequent process of transformation of the principal psychopathological symptoms in the active period. This is followed by gradual reduction of the psychopathological disturbances in the period of stabilisation, culminating in the formation of residual states.

It is important to stress that the concept of slowly progressive schizophrenia developed by A. B. Snezhnevsky is a very important contribution to clinical psychiatry.

But we should point out to Merskey and Shafran the fact that contrary to their statements, the above concept does not represent any essentially new statements that have no analogues in world psychiatry. It represents a phase in the development of teaching about the latent forms of schizophrenia which were started by E. Bleuler (13).

We may assume that the authors are unaware that the study of the benign mild forms of schizophrenia has old roots in Soviet psychiatry (although Shafran, considering the medical education she received in the Soviet Union, should know this). It is enough to point to the research of L. M. Rosenstein (10), N. P. Bruchansky (1) and other authors. But it is hard to imagine that Merskey and Shafran are not up to date on the research into the indistinct forms of schizophrenia which has been conducted outside of the USSR, especially in Western Europe, the USA and Japan (14, 15, 19, 20, 24, 28, 29, 36) from the times of E. Bleuler (13).

Merskey and Shafran meticulously avoid this fact. The main purpose of their article is to show that research on slowly progressive schizophrenia is the internal affair of Soviet psychiatrists, that this research is being conducted only in our country, and thus that it is being done on some special governmental request. In connection with this we would like once again to point to the tenuous position of our opponents. The fact is that slow and relatively benign forms of the endogenous process, quite comparable with most of the varieties of the slowly progressive schizophrenia, are described under different names – ambulatory (36), abortive (25), subclinical (30), and non-regressive (28) schizophrenia – in a whole series of psychiatric publications from the capitalist countries.

In particular, during the '40s to '60s, American psychiatrists investigated the problem of pseudoneurotic schizophrenia intensively (19, 20). Also in the last decades, interest in the indistinct forms of the endogenous disease did not abate in the West. But now the term 'borderline schizophrenia' is used for the definition of such forms. This term has been widely used in the series of clinico-genetic works dealing with the problem of the schizophrenic spectrum (14, 18, 22, 28, 31, 32, 35). We would like to note that the problem of slowly progressive schizophrenia was discussed in the *British Journal of Psychiatry* (23).

All this demonstrates that the views of Merskey and Shafran on the concept of slowly progressive schizophrenia as deliberately designed for political reasons by the Snezhnevsky school and used only in the USSR are totally unsound.

Let us examine another statement of our opponents which is also rather unfounded.

We are talking about the extremely broad diagnosis of slowly progressive schizophrenia which, according to Merskey and Shafran, is being practised by Soviet psychiatrists (we will evaluate their views on the importance and reliability of the diagnosis of some symptoms later).

From what positions do they criticise? The focal point of the reasonings of Merskey and Shafran is the diagnostic criteria of the American clinico-statistical classification of psychiatric diseases - DSM-III.

Let us state right away that DSM-III is a national and not an international classification, and it is in accordance with the diagnostic practice established in the USA. It is not necessary for other national schools, Soviet included, to follow the same nosological classification of psychiatric diseases.

Let us not be distracted however by this, but consider the heart of the matter. The differences between the diagnostic criteria of schizophrenia in DSM-III, which include hallucinations, delusions, profound disorders of thinking, and other symptoms of the first rank (as described by K. Schneider), and the system of clinical parameters used by the Snezhnevsky school in separating slowly progressive schizophrenia, are impressive. The presence of the aforementioned features and some others, characteristic of the symptomatic forms of the disease, is not required for the diagnosis of slowly progressive schizophrenia. But nevertheless, the differences discussed are the proof, according to Merskey and Shafran, of the broader view of slowly progressive schizophrenia practised in our country. The evaluation of a number of psychiatric manifestations which correspond according to the Snezhnevsky classification to the different varieties of slowly progressive schizophrenia seems to these authors highly problematic because of a lack of correlation with DSM-III.

In our opinion such 'proof' can convince only a person with very little knowledge of psychiatry or a biased reader. So, what is the cause of the above discrepancies? Judging by DSM-III, it is not the disagreements between Soviet and American psychiatrists about the boundaries of slowly progressive schizophrenia, but a primarily different approach to the nosological classification of the group of patients defined by this term.

DSM-III reflects the position of investigators treating slowly developing, ill-defined or indistinct forms of schizophrenia as a special type of the disorders of personality - a so-called "schizophrenic character" (34) or "psychotic character" (16). This direction in modern American psychiatry is being developed by R. Spitzer and co-authors (35). In DSM-III, latent, slowly progressive forms of schizophrenia are placed outside the boundaries of the endogenous diseases and in the chapter "Disorders of personality". Accordingly, two parts of this chapter - one (the schizotypal personality disorders) completely and another (borderline personality disorders) partially but considerably - include the different varieties of schizophrenia (latent, simple, pseudoneurotic, residual). The combination of those varieties is comparable with the term 'slowly progressive schizophrenia', which is accepted in the Soviet Union.

The unification of the forms of endogenous nature with the borderline states in DSM-III met with a lot of criticism, some of which emanated from American research workers (31), and it is a matter of discussion presently. But participation in it would lead us too far from the problems we would like to solve in this publication. Returning to the speculations of Merskey and Shafran, let us state that their attempt to define the limits of slowly progressive schizophrenia with the help of the diagnostic criteria from DSM-III seems absurd in the light of the data mentioned above, because it represents the 'trying-out' of the diagnostic model, created for the symptomatic forms on the slowly progressive forms of the disease. (Let us recall that the residual and slowly progressive variants are considered in DSM-III to be "personality disorders" and that schizophrenia is limited to the psychotic forms.) We should point out to Merskey and Shafran that the comparison of the diagnostic criteria for schizophrenia would be correct (considering the differences of the nosological evaluation of the non-symptomatic forms of the disease), only between the DSM-III criteria of schizophrenia and the clinical features of the corresponding symptomatic forms of schizophrenia in accordance with the classification of Snezhnevsky.

What are the diagnostic criteria of the non-manifest variants of schizophrenia? The answer to this question can be given by analysing the clinical parameters sufficient for this diagnosis.

Let us preface the presentation of the clinico-descriptive criteria of slowly progressive schizophrenia by the following thoughts.

The diagnosis of slowly progressive schizophrenia requires a special integral approach, based not on the isolated manifestations of the disease, but on the combination of the clinical features. The attempts to define the limits of slowly progressive schizophrenia based on the models of symptomatic forms, diagnosed mainly by the traditional symptomatological criteria, as in psychoses, may prove fruitless. The doctor will encounter most difficulty in this case in the early phases of the disease, when the psychopathic manifestations are transient and may be seen as separate prodromal symptoms, or may be masked by the psychogenic or somatisation disorders.

The diagnosis of slowly progressive schizophrenia should also take into account the data of premorbid personality, the childhood development, puberty, and adolescence (8). Strange or exotic enthusiasms and abrupt character changes, accompanied by the "undermining of the occupational standard" (27) and changes in lifestyle and activities manifest during these periods are important in the diagnosis of this endogenous form of the process.

The diagnosis is supported by evidence of hereditary predisposition (in cases of familial schizophrenia), and of disturbances in social adaptation. In contrast to the borderline states, a gradual diminution of the ability to work connected to the decline in intellectual activity and initiative is seen in the pathological process. Two levels of psychiatric disturbance should be considered among the pathological features which in our view are used as clinical criteria in the diagnosis of slowly progressive schizophrenia. The first is the disorder characteristic of the endogenous disease from the time of its presentation (I); the second level is disorders in the neurotic, psychopathic and paranoid range which develop and change in ways which are specific to the endogenous process (II).

I.1. Attenuated psychotic symptoms in the context of episodic exacerbations: auditory hallucinations and illusions (commentary voices, command hallucinations, 'thoughts spoken aloud'), hallucinatory transformation of the sensory awareness of oneself [this is a concept in the Soviet literature relating to somatic awareness], olfactory and tactile hallucinations, rudimentary ideas of influence, persecution, special significance, autochthonous delusional perceptions

I.2. Disorders of thought: loss of control of the content and flow of thoughts and images, with a feeling of the thoughts being read [Russian: *mentism*], thought-blocking [Russian: *schperrunge* from the German for jumping], a sudden flood of thoughts, ambivalence [*Ambitendenz*: a word used specifically by Bleuler (1911) for 'ambivalence of the will'], difficulty in forming concepts, blurring of conclusions, reasoning, tendency towards paradoxical constructions, and bizarre ideas

I.3. Negative symptoms (residual state) with profound schizoid changes (deficit of the verschrobene type and others [*verschrobene*: German, meaning odd, very eccentric, often with peculiar ideas], asthenic deficit (asthenic autism)

II.1. Asthenic states acquiring an exaggerated character because of the changes in the intensity of perception (hyperaesthesia, hyperacusis, etc.) where the neurotic symptoms are followed by psychotic impairment (inability to concentrate attention, objective loss of activity, deficiency of motivation and vital energy, apathy)

II.2. Hysterical states in which the conversion or dissociative symptoms are losing their initial demonstrative quality and expressiveness, and have acquired features of personality disorders of the more serious type (hysteroneurotic changing to diffuse somatic hypochondriacal complaints), hysterical anorexia changing to exotic 'vomiting behaviour'; motor hysterical to subcatatonic, a flow of autonomous involuntary images, open to others to read, pseudohallucinations

II.3. Obsessive–phobic states with subsequent transition of the simple phobias to generalised anxiety – phobic states (of the 'madness of doubts' type) [*folie de doute*] with the contrast phobias, obsessive thought with special meaning, phobias of the abstract contents – panphobias, phobophobias, ranging from the elementary obsessive–compulsive disorders to the ruminative obsessive states with the addition of ambivalent ritual behaviour

II.4. Hypochondriacal states with a transition from neurotic and overvalued hypochondria to diffuse hypochondriacal complaints because of the addition of general disturbances of feelings, hypochondriacal illusions, essential hypochondriacal complaints, and symptoms of hypochondriac obsessions, with the phenomenon of alienation of one or another organ

II.5 States of depersonalisation, different from the pattern of neurotic depersonalisation, which are mostly transient, and arise because of the presence of continuous profound disturbances of the sense of self, manifestations of 'autopsychic residual depersonalisation' [a stationary state reflecting a chronic psychosis, the word autopsychic indicating self-awareness and implying an endogenous illness; see introductory note], feeling of the alienation of the higher emotions, recognition of psychological changes of self, deficiency of psychological life, impaired perceptions of reality or contacts with people

II.6. Overvalued thought with the following changes over time in the clinical picture: overvalued ideas – 'overvalued delusions' – systematic paranoid delusions, which are not congruent with the mood or with the predominant affect and which have paradoxical content detached from reality

II.7. Psychopathic states with distorted constitutional character structure as a result of the change or addition of the schizoid element and subsequent dynamics of the evolving schizoid type (gradual impoverishment of the emotional sphere, mainly higher emotions, an alteration in judgement and feeling such that higher feelings are lost and mutually incompatible thoughts held without affective conflict because of the inability to relate thoughts to the emotional content, increasing withdrawal with pathological autistic activity, inadequacy of behaviour and appearance).

Returning to the analysis of the publication by Merskey and Shafran, let us recognise that the above diagnostic criteria allow us to decline the statement of these authors that the tendency to classify psychiatric disorders of another nature under slowly progressive schizophrenia is ostensibly peculiar to the Snezhnevsky school. Merskey and Shafran try to persuade the reader that Soviet psychiatrists are not only widening the limits of slowly progressive schizophrenia with respect to borderline pathology, but also liberally diagnose healthy people with this disease.

If we set aside general statements of a propagandistic character (their analysis is not our purpose) and attend to the clinical material on a strictly scientific basis, we can see that the authors do not have any convincing arguments to prove their assertions.

Let us analyse the system of evidence used by Merskey and Shafran. On multiple occasions they stress that togther with clear-cut psychopathological syndromes a number of states devoid of the features characteristic of the active process are mentioned in the pages of the *Korsakoff Journal* among the clinical characteristics of slowly progressive schizophrenia.

One wonders why Merskey and Shafran are interested in these data. We are dealing with everyday clinical practice: non-specific manifestations, which might appear (caused by traumatic life events) in psychologically healthy individuals, also may be the most vivid manifestation during certain phases of the development of the disease (latent period, remission, residual states). The fact that some pathological phenomena seen in psychiatric patients may be seen in healthy people is widely known both in the USSR and abroad. It is known (according to English textbooks of psychiatry) to Merskey and Shafran as well. But with the help of rather pretentious constructions they ascribe a very special meaning to this fact.

The thoughts of Merskey and Shafran evolve approximately according to the following scheme: at first, they try to stress the wide distribution of certain kinds of disturbances in the population, illustrating it by quite short quotations from the Soviet authors ("brief disorders of the concentration of attention", "pronounced emotional lability", "withdrawal", etc.). Merskey and Shafran point out that such states are peculiar also to "the multitude of people who might not be considered as psychiatric patients" (26). The interpretation of the clinical characteristics is done in a similar manner. Commenting on such quotations from the general contents as "profound optimism", "limitless belief in one's abilities", etc., Merskey and Shafran note: "These features might characterise some very successful members of any group".

Then (with the help of a seemingly innocent logic of operation) Merskey and Shafran make the next move – change the clinical emphasis. Their train of thought could be seen as a kind of proof from the opposite: if some symptoms can be seen in healthy individuals, they should not necessarily be classified as pathological. As a result they offer a new view on problems which contradict clinical reality: they equate the psychological norm with the pathological psychic activity (albeit indistinct).

In reality, even if we detach ourselves from the phenomenological differences, these manifestations are not comparable either in the mechanism of formation or in their dynamics. Psychopathological symptoms, seen in normal individuals, in contrast to the perceptions, imaginations, thoughts related to their normal psychological life, appear only under special circumstances (extreme, conflict, etc.). Besides, as a rule in such cases, the loss of the psychiatric equilibrium is transient. According to

Rumke (33), disturbances in healthy people tend to be very transient whether they are disorders of perception (illusions, hallucinations) self-referential ideas, obsessions, derealisation or other phenomena.

But, according to Merskey and Shafran, if people who were diagnosed with slowly progressive schizophrenia develop the symptoms which are not necessarily considered to be a feature of the disease, they might be psychologically well. ("Soviet psychiatrists describe many phenomena as pathological," write Merskey and Shafran, "although by themselves these phenomena are not pathological" [*sic*].)

It seems to us that there is no sense in arguing with such considerations, especially because every clinically sound psychiatrist understands that in the case of the distinction between sickness and health, the evaluation of separate symptoms is not the final point. Even if at the time of evaluation the clinical picture is completely dominated by the manifestations which, according to Merskey and Shafran, are characteristic of healthy people, it is not sufficient either to reject the assumption that the slow endogenous process is taking place, or to accept it. The diagnosis of slowly progressive schizophrenia (this point was discussed above) requires the integration of various sets of data, including the anamnesis.

Towards the end of the discussion we would like to comment on another characteristic of our opponent's article. The dismissive attitude towards Soviet psychiatry sounds like an undercurrent, but quite distinctly in all of their remarks Merskey and Shafran doubt several provisions made by the scientific school of A. B. Snezhnevsky, stressing how unacceptable they are to the Western world. In reality that is wrong. The problems of schizophrenia have been discussed on multiple occasions in symposia of the WHO and other international organisations during the last decade. Both Soviet and Western psychiatrists participated in them. Despite differences in the nosological systems and possible discrepancies in diagnostic evaluations, the foreign colleagues regarded the results of the clinical investigations done in the USSR with interest and understanding. Merskey and Shafran regret that Soviet physicians who do not use the nosological standards accepted in Canada, England, and the USA make mistakes in clinical practice (in particular, they widen the diagnostic framework of slowly progressive schizophrenia).

It seems to us that the authors have lost their sense of reality again. Do they really think that only specialists of a Western orientation can evaluate the clinical manifestations correctly, and that the physicians (Soviet included) practising outside the Western psychiatry are totally helpless in practical and research ability?

It is reasonable to remind Merskey and Shafran of the following. The history of psychiatry shows that despite inevitable divergence between different national schools in the interpretation of different problems which are important at the present level of scientific development, any of them may contribute important data objectively promoting progress. Only scientific impartiality with strict clinical analysis of the facts presented by the opponents and not a biased approach, pursuing questionable political purposes, can promote the successful solution of the problem of slowly progressive schizophrenia.

References

1. Bruhansky N.P. On the problem of schizophrenias. Moscow, 1934, p. 8.
2. Vorob'ev V.U., Nefed'ev O.P. Rehabilitation of patients with neuropsychiatric disorders and alcoholism. Leningrad, 1986, pp. 176–177.
3. Gorchakova L.N., Il'icheva V.I. Rehabilitation of patients with neuropsychiatric disorders and alcoholism. Leningrad, 1986, pp. 180–182.
4. Dubnizkaya E.B. On the clinical specifics of the syndrome of hysterical hypochondria. J. Neuropathol. Psychiatr., 1977, 5:733–738.
5. Kerbikov O.V. Modern problems of schizophrenia. Moscow, 1933, pp. 97–111.
6. Korkina M.V., Zivil'ko M.A., Marilov V.V. Nervous anorexia. Moscow, 1986.
7. Lakosina N.D. Clinical variants of the neurotic development. Moscow, 1970.
8. Lichko A.E. Psychiatry of adolescence. Leningrad, 1985.
9. Nadzharov R.A. Schizophrenia: Multidiscipline research. Editor: A.V. Snezhnevsky. Moscow, 1972, pp. 33–36.
10. Rosenstein L.M. Problems of the mild forms of schizophrenia. Moscow, Leningrad, 1933.
11. Fridman B.D. On the mild forms of schizophrenia. Sov. Neuropathol., Psychiatr. Psychohygiene, 1934, 3, 5:14–26.
12. Berner P. Psychiatrische Systematik. Bern, 1977.
13. Bleuler E. Dementia praecox oder Gruppe der Schizophrenien. Leipzig, 1911.
14. Chihara S., Yoneda H., Sacai T. Bull. Osaca med. Sch., 1983, Vol. 29 (2). pp. 106–120.
15. Ey H., Bernard P., Brisset Ch. Manuel de psychiatrie. Paris, 1967.
16. Frosch J. Psychiat. Quart., 1964, Vol. 38. pp. 81–96.
17. Glatzel J. Fortschr. Neurol. Psychiat., 1972. Bd 40. pp. 596–619.
18. Heston L. Science, 1970. Vol. 167. pp. 249–256.
19. Hoch P.H., Cattell P., Strahl M., Pennes H. Amer. J. Psychiat., 1963. Vol. 119. pp. 106–115.
20. Hoch P., Polatin J. Psychiat. Quart., 1949. Vol. 23. pp. 248–278.
21. Huber G. Psychiatrie: Sistematischer Lehrtext fur Studenten und Arzte. Stuttgart, 1981.
22. Kety S.S. Genetics of neurological and psychiatric disorders. Eds. S.S. Kety et al. New York, 1983. pp. 105–114.
23. Khouri Ph., Haier R., Rieder R., Rosenthal D. Brit. J. Psychiat., 1980. Vol. 137. pp. 140–147.

24. Kronfeld A. Nervenarzt., 1928. Bd. 179. pp. 46–51.
25. Mayer W. J. Nerv. Ment. Dis., 1950. Vol. 112. pp. 539–542.
26. Merskey H., Shafran B. Brit. J. Psychiat., 1986. Vol. 148. pp. 247–256.
27. Mundt Ch. Nervenarzt., 1983. Bd 54. pp. 131–138.
28. Nyman A.K. Acta Psychiat. Scand., 1978. Suppl. 172.
29. Pascal C. La Demence precoce. Paris, 1911.
30. Peterson D.R. J. Consult. Psychol., 1954. Vol. 18. pp. 198–200.
31. Pope H., Jonas, J., Hundson J. et al. Arch. Gen. Psychiatr., 1983. Vol. 40. pp. 23–36.
32. Rosenthal D. Genetic theory and abnormal behaviour. New York, 1970.
33. Rumke H. C. Eine bluhende Psychiatrie in Gefahr. Berlin, 1967. pp. 126–134.
34. Schafer R. The clinical application of psychological tests. New York, 1948. pp. 218–223.
35. Spitzer R., Endicott J., Gibbon M. Arch. Gen. Psychiat., 1979. Vol. 36. pp. 17–24.
36. Zilboorg G. Psychiatry, 1941. Vol. 4. pp. 149–155.

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Comments on 'Slowly Progressive Schizophrenia' by A. B. Smulevitch

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In the preceding translation we tried to provide a literal rendering of the complete original article, changing it only for purposes of clarity or comprehensibility. We now offer our own judgements of the content of the article. We have made them short because we believe most of the problems with the article by Smulevitch will be readily evident to anyone who normally has access to the *British Journal of Psychiatry*, and who may compare our original article (Merskey & Shafran, 1986) with the content of the Smulevitch one.

Smulevitch espouses two main themes. The first is that we use a tendentious, unscientific approach to claim that Soviet authors widen the diagnostic framework of schizophrenia by using the term 'slowly progressive schizophrenia'. We termed this 'sluggish schizophrenia', as is common in the West, but it is perhaps better called 'slowly progressive schizophrenia'. We outlined this concept in the introductory notes. We believe that it crumbles to dust in the light of the evidence we shall examine.

Secondly, Smulevitch claims that we wrongly deny the existence of Western analogues to slowly progressive schizophrenia, other than pseudoneurotic schizophrenia, which is largely defunct, and simple schizophrenia or defect states, which have a restricted meaning and are not often diagnosed. He then refers to 23 sources from outside the USSR in support of the claim that slowly progressive schizophrenia is recognised under different terms.

Most of these authors are held to be interested in the vague (or ill-defined) forms of schizophrenia, or to have studied 'borderline schizophrenia' in clinical genetic investigations. We have reviewed the first 20 of these available to us so far.

Two of the references are to Hoch & Polatin (1949) and Hoch *et al* (1962) (cited by Smulevitch as 1963), and a third to Mayer (1950). They deal with pseudoneurotic schizophrenia. He is correct in recognising that we observed the notion to be defunct nowadays in the West. Also, the interest of most or all of those American workers who have dealt with personality traits or features related to character was coupled with the recognition that the patients were usually in touch with reality. Frosch (1964), a writer with a marked psychodynamic emphasis, observes, "... there are basic differences which establish that these people are generally not psychotic. Foremost among these is that the capacity to test reality, while often very defective and manifesting primitive qualities, is, nonetheless, relatively intact." Peterson (1954), who is also quoted from that period, wanted to use the Minnesota Multiphasic Personality Inventory to recognise subclinical schizophrenia or predict its future appearance. His position can fairly be compared to that of Dr Smulevitch in terms of looking for phenomena which are not immediately manifest, but it is limited to psychological test material. His method would not be usable to determine the presence of an illness requiring compulsory detention in hospital.

Schafer (1948) likewise relies on psychological tests. The example cited of "Schizophrenic character disorder" (pp. 218–233) would probably not qualify even as a schizotypal personality under DSM–III–R (American Psychiatric Association, 1987).

Kronfeld (1928) describes two co-operative patients with cyclical illnesses, quite like bipolar disorders. Kronfeld's emphasis on insight, improvement, and psychotherapy are not part of the concept of slowly progressive schizophrenia which we found in the Soviet literature. Also, his diagnoses of 'schizophrenia mitis' or weak schizophrenia would probably not be acceptable today. The title of his article may have fitted well with Dr Smulevitch's argument, but the rest of it does not, even though Kronfeld was considered by Snezhnevsky to have been his mentor.

Both Rosenthal (1970) and Kety *et al* (1983) endeavoured to use a broad-spectrum concept of schizophrenic illness. Their purpose was to recognise phenomena related to schizophrenia in the relatives of probands. Heston (1970) adopted a similar approach. None of their writings suggest that these authors were interested in diagnosing schizophrenia as a clinical event for hospital admission or treatment on the basis of minimal signs among the relatives of their typically schizophrenic patients. Indeed, Kety, in his most recent article on schizophrenia spectrum disorders, directs his comments to the theme of "non-psychotic variants of schizophrenic psychopathology" (Ingraham & Kety, 1988).

Henri Ey is cited by Smulevitch from the 1967 edition of his book (Ey *et al*, 1978). We have had access to the later version. Ey recognises evolution of some schizophrenic illness and notes that Bleuler widened the concept of schizophrenia (p. 535). He observes that Bleuler's synthesis was successful but ". . . by dropping precise criteria [chronicity and flattening - literally *évolution chronique et démence affective*] the notion of schizophrenia became open to be used, almost without any limit". The marginal summary for this paragraph reads "extension abusive du groupe après que celui-ci ait perdu son critère évolutif". We can translate this charitably as a comment on an "improper extension". Ey does recognise forms which do not evolve and do not show defect (p. 589), and he calls them *"Formes mineures"*. He also says (p. 596), "It is almost always possible, although often very difficult, to establish discrete delusional or hallucinatory activity not recognized by his entourage". He also recognised the occurrence of schizoneuroses or schizoid personalities with neurotic or psychotic episodes. It does not appear to us that he seems to be willing to accept the idea of slowly progressive schizophrenia on the basis of this category.

Rumke (1967) is cited tangentially by Dr Smulevitch. It is somewhat ironic that in the same volume, Rumke (p. 203) talks about the definition of schizophrenia and observes that the most important thing is to differentiate real from pseudoschizophrenia. Rumke emphasises the importance of differentiating other diagnoses which might be confused with schizophrenia, including manic-depressive illness and degenerative and paranoid states, and quotes Mayer Gross, who points out that some patients can be psychotic for a while, but do not have "real schizophrenia". Likewise, cerebral organic disorders have to be distinguished, as do others which cannot be categorised, such as psychoses with epilepsy. He says that it is very important not to make the diagnosis of schizophrenia in these cases, and even the term 'pseudoschizophrenia' can be dropped. We wonder whether Dr Smulevitch was well acquainted with this particular source.

Some of the more recent articles cited deal with borderline personality disorder and borderline schizophrenia, e.g. Spitzer *et al* (1979), Khouri *et al* (1980) and Pope *et al* (1983). Smulevitch recognises that that is seen as a controversial topic in the West. Those articles just mentioned are all from the United States, although one was published in the *British Journal of Psychiatry*. None of them mentions slowly progressive schizophrenia as a concept by name, although Smulevitch says that the one in the *British Journal of Psychiatry* does so. The aim in these studies is to examine the validity of the groupings of borderline personality disorder and borderline schizophrenia or closely similar concepts. Chihara *et al* (1983) write about "borderline cases", but 21 of their 30 patients had schizotypal personality disorder. All these authors aim to distinguish the phenomena under consideration from schizophrenia or show if they are identical with it. It is markedly inappropriate to use the articles in question as proof of an identity with the Soviet concept of a subtle progressive disease. All four present operational criteria and all compare their groups with recognised schizophrenia.

Mundt (1983) reports on apathy in 257 chronic schizophrenic patients, and examines factors relating to it, such as pre-morbid personality, the characteristics of the episodes of illness (such as affective status and time course), ageing, and the size of the ventricles. Curiously, the dosage of neuroleptics is omitted. Smulevitch claims that Mundt studied slowly progressive schizophrenia. That is not apparent in our understanding of Mundt's text.

The Swedish study on non-regressive schizophrenia (Nyman *et al*, 1978; Nyman, 1978) relates to patients with pictures like those of pseudoneurotic schizophrenia or 'borderline' conditions. However, Nyman *et al* state "these patients most often feel quite clearly a distinct sense of having caught a disease", hardly a feature of slowly progressive schizophrenia as diagnosed in dissenters. The relevance of this version of schizophrenia to Dr Smulevitch's claims is not evident. Among the other citations by Smulevitch, Zilboorg (1941) offers a sketchy, unsubstantiated, and probably unethical series of comments on three named murderers who were executed (clearly some horrors are preserved in our own earlier literature). Incidentally, as a Russian *emigré*, Zilboorg appears also to be transmitting some of Serbsky's opposition to Kraepelin's concept of schizophrenia as an irrecoverable dementia.

It appears that the sources to which Smulevitch refers, and which we have examined, do not support his claims. Most are outdated and only half are from the last two decades, during which time considerable advances have taken place internationally in the diagnosis of schizophrenia. The borderline syndromes in the papers which he quotes usually do not resemble current Soviet descriptions of slowly progressive schizophrenia, as reviewed in our previous paper (Merskey & Shafran, 1986). They are no longer conceived of by many as schizophrenic. Quite a few remit. Many of the patients have insight. Delusions are often present temporarily at least. Some Western and Japanese authors are interested in these poorly defined cases in order to determine the associations of the genetic patterns of schizophrenic illness. None sees them as diagnostically identical with schizophrenia, even if a possible biological unity is being explored.

The citation of other authors appears tangential. Some, like Mundt, have reported on overt classic cases of chronic schizophrenia, and do not treat premorbid personality, as claimed by Smulevitch. We have noted already the mis-statement about Khouri and the *British Journal of Psychiatry*.

The recent authors who deal with conditions that might be linked with schizophrenia give systematic criteria that differ significantly from those of Dr Smulevitch, so far as the latter can be defined. In fact, the Western or Japanese authors frequently observe the presence of overt hallucinations in their so-called ill-defined cases.

Perhaps the strongest support for the ideas relating to slowly progressive schizophrenia can be traced to Bleuler. Bleuler (1911) emphasised the occurrence of simple schizophrenia, which, among other things, was accompanied by affective change and eccentricity (pp. 235–239), and he even argued that the 'latent' illness was the commonest form. Besides that, he greatly extended the boundaries of the diagnosis of schizophrenia to include many cases with prominent manic features. Bleuler probably promoted quite widespread misdiagnosis of simple schizophrenia and schizophrenia, when depression, personality disorder, or mania would have been more suitable diagnoses.

Bleuler appears to have had a considerable influence upon the broader criteria of schizophrenia in American psychiatry which have subsequently been renounced, most strikingly with DSM–III (American Psychiatric Association, 1980). Western psychiatrists, as exemplified in DSM–III, now demand very much more solid evidence for the diagnosis of the disorder. Simple schizophrenia by name has disappeared from DSM–III–R (American Psychiatric Association, 1987). In any case, the loose system of diagnosis which Dr Smulevitch is attempting to support from the Western literature has been outmoded there for more than 15 years and severely criticised. It is scarcely the best proof of continuing Western support for related ideas, although Vartanyan (1988) is reported by Tass as defending the Soviet use of the diagnosis of slowly developing schizophrenia on the grounds that it was described for the first time by Hoch and Polatin in America in 1941 (sic).

Berrios (1987, p. 206) points out that Bleuler's approach was bound to result "in an inordinate number of false positives . . . [and] a pliable and overwide concept of schizophrenia". Berrios indicates that Bleuler's broad approach was promptly and widely neglected in France, and he notes also that the Schneiderian backlash put an end to his concept of schizophrenia.

In the wide-ranging samples of both the Western literature and the Soviet literature which Dr Smulevitch has considered, there is one notable omission. Kazanetz (1979), a Moscow psychiatrist, published a large systematic follow-up of 312 patients in which he examined the usefulness of the diagnosis of slowly progressive schizophrenia. According to Kazanetz, "These criteria associated with the Snezhnevsky school, referred to as the Moscow school in the USSR, over-extend the diagnosis of schizophrenia . . . ." Retrospective rediagnosis from the initial data, both by three clinicians and by a computer program, agreed in 97% of cases. These rediagnoses were validated, indeed vindicated, by the follow-up data. Of those rediagnosed as having exogenous or non-schizophrenic psychoses, only 23% received such a diagnosis originally. Kazanetz observes that such overdiagnosis of schizophrenia was "primarily a result of adherence to the kind of criteria applied by the Moscow school for classifying psychosis". If the previous practice at the Gannushkin Hospital is representative of acceptable standards of practice in the diagnosis of slowly progressive schizophrenia, then the findings of Kazanetz must be taken to demolish the usefulness of, or justification for, the concept.

In our previous article (Merskey & Shafran, 1986) we objected to the failure of the Soviet literature to deal adequately with the sources, to produce clear descriptions, to provide satisfactory factual data, and to undertake reliability studies. Dr Smulevitch has not remedied these defects, and we consider that he has repeated them. The problem of the diagnosis of slowly progressive schizophrenia or sluggish schizophrenia in Moscow was well described by Kazanetz in 1979, and was recognised by the WHO in its international pilot study of schizophrenia as long ago as 1973 (World Health Organization, 1973). American practice, which was also seen to be faulty in those days, has clearly changed.

Even the diagnoses which were current in the United States do not support the position of Dr Smulevitch that these conditions were established and recognised as valid in the West. For example, DSM–I does not mention them, while DSM–II gives the following characteristics:

> "295.5 Schizophrenia, latent type.
>
> This category is for patients having clear symptoms of schizophrenia but no history of a psychotic schizophrenic episode. Disorders sometimes designated as

> incipient, pre-psychotic, pseudoneurotic, pseudopsychopathic, or borderline schizophrenia are categorized here.”

This is as near to accepting pseudoneurotic schizophrenia or anything like slowly progressive schizophrenia as the official American literature ever seems to have gone. It was, of course, radically changed for DSM–III.

One last, over-riding consideration is never examined by Smulevitch. Psychotic character and latent psychotic phenomena are not acceptable in the West as grounds for compulsory admission to hospital. The Royal College of Psychiatrists has concluded that there is good evidence that a number of Soviet psychiatrists in prominent positions have engaged in political abuse of psychiatry. Many of the victims were labelled as having slowly progressive schizophrenia. None of the diagnoses which Smulevitch has cited from the West can be used currently to detain an individual in hospital against his wishes. So far as we can determine, individuals are still held against their wishes in hospital, in the USSR, with that label. The point is ignored by Dr Smulevitch, although some Soviet writers have tackled it vigorously, e.g. Tsaregorodtsev (1988), who remarks in one of his mildest comments: “One and the same person may be diagnosed as a deranged, irresponsible schizophrenic in Moscow and as quite healthy in Leningrad or Kiev.”

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References

American Psychiatric Association (1980) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn) (DSM–III). Washington, DC: APA.

—— (1987) *Diagnostic and Statistical Manual of Mental Disorders*. (3rd edn, revised) (DSM–III–R). Washington, DC: APA.

Berrios, G. E. (1987) Commentary on extracts from Bleuler (1911). In *The Origins of Modern Psychiatry* (ed. C. Thompson). pp. 200–209. London: Wiley.

Bleuler, E. (1911) (trans. 1950) J. Zinkin. New York: International Universities Press.

Chihara, S., Yoneda, H., & Sakai, S. (1983) Clinico-genetic study of a so-called borderline case. *Bulletin of the Osaka Medical School*, **29**, 106–120.

Ey, H., Bernard, P. & Brisset, Ch. (1978) *Manuel de Psychiatrie*. Paris: Masson.

Frosch, J. (1964) The psychotic character: clinical psychiatric considerations. *Psychiatric Quarterly*, **38**, 81–96.

Heston, L. L. (1970) The genetics of schizophrenic and schizoid disease. *Science*, **167**, 299–256.

Hoch, P. H., Cattell, J. P., Strahl, M. O., *et al* (1962) The course and outcome of pseudoneurotic schizophrenia. *Psychiatric Quarterly*, **119**, 106–115.

—— & Polatin, P. (1949) Pseudoneurotic forms of schizophrenia. *Psychiatric Quarterly*, **23**, 248–278.

Ingraham, L. J. & Kety, S. S. (1988) Schizophrenia spectrum disorders. In *Handbook of Schizophrenia*, vol. 3, *Nosology, Epidemiology and Genetics* (eds M. T. Tsuang & J. C. Simpson), pp. 117–137. North Holland: Elsevier.

Kazanetz, E. Ph. (1979) Differentiating exogenous psychiatric illness from schizophrenia. *Archives of General Psychiatry*, **36**, 740–745.

Kety, S. S., Rowland, L. P., Sidman, R. L., *et al* (eds) (1983) *Genetics of Neurological and Psychiatric Disorders*. New York: Raven Press.

Khouri, P. J., Haier, R. J., Rieder, R. O., *et al* (1980) A symptom schedule for the diagnosis of borderline schizophrenia: a first report. *British Journal of Psychiatry*, **137**, 140–147.

Kronfeld, A. (1928) Some comments on schizophrenia mitis, mainly from the psychotherapeutic aspect. *Nervenarzt*, **179**, 46–51.

Mayer, W. (1950) Remarks on abortive cases of schizophrenia. *Journal of Nervous and Mental Diseases*, **112**, 539–542.

Merskey, H. & Shafran, B. (1986) Political hazards in the diagnosis of ‘sluggish schizophrenia’. *British Journal of Psychiatry*, **148**, 247–256.

Mundt, C. (1983) The syndrome of residual apathy in schizophrenia. A psychopathological long-term study. *Nervenarzt*, **54**, 131–138.

Nyman, A. K. (1978) Non-regressive schizophrenia. Clinical course and outcome. *Acta Psychiatrica Scandinavica* (suppl. 272).

Nyman, G. E., Nyman, A. K. & Nylander, B. I. Non-regressive schizophrenia. *Acta Psychiatrica Scandinavica*, **57**, 165–192.

Peterson, D. R. (1954) The diagnosis of subclinical schizophrenia. *Journal of Consulting Psychology*, **18**, 198–200.

Pope, H. G., Jonas, J. M., Hudson, J. I., *et al* (1983) The validity of DSM–III borderline personality disorder. *Archives of General Psychiatry*, **40**, 23–30.

Rosenthal, D. (1970) *Genetic Theory and Abnormal Behavior*. New York: McGraw-Hill Book Co.

Rumke, H. C. (1967) III. Beitrage zur Psychologie and Psychopathologie. Die psychischen Storungen des gesunden Menschen. In *Eine bluhende Psychiatrie in Gefahr*, pp. 126–134. Berlin: Springer-Verlag.

—— (1967) IV. Uber die Schizophrenie. Die klinische Differenzierung innerhalb der Gruppe der Schizophrenien. In *Eine bluhende Psychiatrie in Gefahr*. Berlin/Heidelberg/New York: Springer-Verlag, pp. 204–211.

Schafer, R. (1948) *The Clinical Application of Psychological Tests*. Menninge Foundation Monograph Series. New York: International Universities Press.

Spitzer, R. L., Endicott, J. & Gibbon, M. (1979) Crossing the border into borderline personality and borderline schizophrenia. *Archives of General Psychiatry*, **36**, 17–24.

Tsaregorodtsev, M. G. (1988) The horrors of Soviet psychiatry. *Toronto Globe & Mail*, 30 June, A7.

World Health Organization (1973) Report on The International Pilot Study of Schizophrenia. Vol. 1: Results of the Initial Evaluation Phase. Geneva: World Health Organization.

Vartanyan, M. (1988) *Tass* (in English), 24 May.

Zilboorg, G. (1941) Ambulatory schizophrenia. *Psychiatry*, **4**, 149–155.

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The Factor Structure of the General Health Questionnaire (GHQ-30)

A Reliability Study on 6317 Community Residents

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An individual's responses to Goldberg's 30-item General Health Questionnaire are usually represented as a single score which provides a measure of the number of psychiatric symptoms reported. No account is taken of the nature of the symptoms. Factor analyses of the GHQ-30 were undertaken in ten randomly selected samples of 600 adults each, and also on 12 age–sex groupings covering the age range 18–98. The results indicate an impressive degree of consistency of the factor structure, and the identification of five distinct factors corresponding to anxiety, feelings of incompetence, depression, difficulty in coping, and social dysfunction.

The instrument of choice for screening psychiatric disorder in patient and community samples is the General Health Questionnaire (GHQ; Goldberg, 1972). The widespread use of this instrument means that methods for increasing the amount of information yielded by the questionnaire would be of great value in advancing research. The traditional way of scoring the GHQ is to rate each response in terms of whether the symptom is present or absent, and to sum the number of symptoms. Although this simple, additive approach is useful as a measure of the number of psychiatric symptoms declared by an individual, it neglects qualitative aspects of the data, i.e. the nature of the symptoms. The list of questions in the GHQ covers many different types of behaviour, including sleep patterns, worries, relationships, depressed mood, etc. Therefore, it may be possible to derive subscales, each concerned with a particular type of symptom, and subsequently to derive a score for each individual on each of these subscales.

An objective approach to deriving subscales is factor analysis. This is a statistical method for determining which items cluster together to form 'factors'. Sometimes factors are easy to interpret, because the items in the cluster bear a meaningful relationship to each other. At other times it is difficult to understand why a group of items cluster together to form a factor. One reason why interpretative difficulties often arise following factor analysis is limited sample size. When a sample is small, random fluctuations can have a marked effect. Moreover, with small samples, it is rarely possible to examine the reliability of the factor structure.

The exceptionally large database which we have established provides a unique opportunity to investigate the factor structure of the GHQ. We administered the GHQ to an adult sample of the British population participating in the Health and Lifestyle Survey (Cox *et al*, 1987). The survey collected a great deal of information on physical health and health-related behaviour. In selecting an instrument to measure mental health we wanted to focus on psychological and psychosocial symptoms rather than somatic symptoms. For this reason we selected the 30-item version of the GHQ (GHQ-30), which was derived from the original 60-item version by excluding symptoms that were commonly present in subjects with entirely physical illness. The other version which we considered was the GHQ-28, which has been derived from the GHQ-60 on the basis of factor analysis. A quarter of the items in the GHQ-28 are concerned with somatic symptoms and a further quarter with severe depression, which we felt to be unsuitable for a normal population sample.

The number of respondents who completed the questionnaire was 6317, which is by far the largest sample ever studied with this instrument, and is a good representation of the British population (see below). Basic descriptions of the GHQ scores and their relationship to socio-demographic and other variables are available elsewhere (Huppert *et al*, 1987). A comparative study of the conventional GHQ score and a score taking account of chronic symptoms (CGHQ) has also been reported on this population sample (Huppert *et al*, 1988).

Method

The 30-item GHQ was introduced to respondents in their own home by a nurse at the conclusion of a series of physiological measurements and simple tests of cognitive function (see Cox *et al*, 1987; Huppert *et al*, 1987). The nurse's visit was the second phase of the Health and Lifestyle Survey and took place 1–2 weeks after an extensive initial interview. The GHQ was accepted by 7304 participants, who were instructed to complete it on their own and return it in a stamped, addressed envelope. The questionnaire was returned by mail by 6572 participants (88.6%). Only complete questionnaires were analysed, the final figure being 6317 (86.5%). To determine if the sample was representative of the British population, the age and sex distribution of our sample was compared with figures from the 1981 census (Blaxter, 1987). Overall, our sample was found to be a good representative sample, with the exception of men aged 18–29, who were under-represented (21.3% *v.* 24.8%), as were women aged 70 plus (9.2% *v.* 16.2%).

The first factor analysis was carried out on a randomly selected sample of 6000 individuals which was taken from the complete database of 6317 individuals. The size of this sample was adjusted for the convenience of the following subsampling. These 6000 individuals were then randomly allocated to one of 10 subsamples of 600 adults, and factor analyses were carried out on each of the 10 subsamples. Factor analyses were also carried out on the 12 groups of individuals obtained when the main sample of 6000 was divided by sex and by age into the following groupings: 18–24, 25–34, 35–44, 45–54, 55–64, 65+. These last analyses were carried out in order to explore any variation in factor structure due to sex and/or age.

Orthogonal varimax rotation facilitates the identification of factors that are uncorrelated. Although this can simplify interpretation of what the factors mean, it is likely that in the real world factors are correlated. For this reason the factor analysis on the whole sample was repeated using an 'oblimin' (oblique) rotation which does not retain the orthogonality of the factors. All analyses were carried out on the raw data (Likert scores).

Results

It should be appreciated at the outset that there will always be a measure of subjectivity in the number of factors selected, and in the items considered to be making an important contribution to a factor. This is an inevitable result of the data set containing no *a priori* classification of either cases or items. The criterion for identifying

TABLE I

Varimax rotated factor structure of the GHQ-30 (n = 6000)[1,2]

Item		*Factor*				
		A	*B*	*C*	*D*	*E*
1	Could not concentrate	39	45	01	09	15
2	Lost sleep	*66*	10	09	09	08
3	Restless nights	11	−09	01	38	17
4	Not busy or occupied	−04	*59*	22	01	28
5	Not out of the house	15	39	02	03	*54*
6	Not managing well	09	*55*	18	08	00
7	Not doing things well	24	*75*	07	06	05
8	Not satisfied with task	20	*74*	02	13	05
9	No warmth and affection	13	12	09	03	15
10	Could not get on with others	14	07	12	06	*61*
11	Not chatting with others	09	08	06	09	*79*
12	Not playing a useful part	11	48	26	07	45
13	Could not make decisions	04	16	06	*50*	07
14	Felt under strain	*82*	06	00	09	06
15	Could not overcome difficulties	*68*	20	22	13	03
16	Found life a struggle	21	02	04	*69*	04
17	Not enjoying activities	05	12	−10	*66*	04
18	Taking things hard	*72*	05	11	14	07
19	Scared or panicky	27	03	22	*55*	−03
20	Could not face problems	25	34	36	09	07
21	Felt everything on top	*80*	13	17	12	07
22	Unhappy and depressed	*75*	15	28	09	10
23	Lost confidence	*62*	23	41	08	08
24	Felt worthless	44	20	*61*	04	08
25	Felt life hopeless	21	00	*59*	42	−03
26	Not hopeful about future	15	23	*53*	11	17
27	Not feeling happy	01	04	27	*61*	−01
28	Nervous and strung up	*75*	12	30	11	05
29	Felt life not worth living	36	12	*70*	04	10
30	Nerves too bad	49	17	*52*	05	06
% variance accounted for		28.9	7.6	6.2	4.1	3.8

1. Loadings greater than 0.5 are in italics.
2. All decimal points on loadings are omitted.

TABLE II

Items making a significant contribution to GHQ factors

Factor[1]	*Total variance accounted for in subsamples (%)*	*Order of items*[2,3]		*GHQ item*		*Factor loadings for whole sample*
		Whole sample	*10 subsamples*			
A	26.6–31.2	1	1	14	Felt constantly under strain?	0.82
		2	2	21	Found everything getting on top of you?	0.80
		3	3	28	Been feeling nervous and strung-up all the time?	0.75
		4	4	22	Been feeling unhappy and depressed?	0.75
		5	5	18	Been taking things hard?	0.72
		6	6	15	Felt you couldn't overcome your difficulties?	0.68
		7	7	2	Lost much sleep over worry?	0.67
		8	8	23	Been losing confidence in yourself?	0.63
		(9)	(9)	(30)	Found at times you couldn't do anything because your nerves were too bad?	(0.49)
		(10)	(10)	(24)	Been thinking of yourself as a worthless person?	(0.44)
B	7.2–8.3	1	1	7	Felt on the whole you were doing things well?	0.75
		2	2	8	Been satisfied with the way you've carried out your task?	0.74
		3	4	4	Been managing to keep yourself busy and occupied?	0.59
		4	3	6	Been managing as well as most people would in your shoes?	0.55
		(5)	(5)	(12)	Felt that you are playing a useful part in things?	(0.48)
		(6)	(7)	(1)	Been able to concentrate on whatever you're doing?	(0.45)
		(7)	(6)	(5)	Been getting out of the house as much as usual?	(0.39)
C	5.2–6.8	1	1	29	Felt that life isn't worth living?	0.70
		2	2	24	Been thinking of yourself as a worthless person?	0.61
		3	3	25	Felt that life is entirely hopeless?	0.59
		4	4	26	Been feeling hopeful about your own future?	0.53
		5	5	30	Found at times you couldn't do anything because your nerves were too bad?	0.52
		(6)	(6)	(23)	Been losing confidence in yourself?	(0.41)
D[4]	3.9–5.0	1	1	16	Been finding life a struggle all the time?	0.69
		2	2	17	Been able to enjoy your normal day-to-day activities?	0.66
		3	3	27	Been feeling reasonably happy, all things considered?	0.61
		4	4	19	Been getting scared or panicky for no good reason?	0.55
		5	5	13	Felt capable of making decisions about things?	0.50
		(6)	(7)	(25)	Been feeling that life is entirely hopeless?	(0.43)
		(7)	(6)	(3)	Been having restless, disturbed nights?	(0.38)
E	3.5–4.0	1	1	11	Spent much time chatting with people?	0.80
		2	2	10	Been finding it easy to get on with other people?	0.61
		3	3	5	Been getting out of the house as much as usual?	0.54
		(4)	(4)	(12)	Felt that you are playing a useful part in things?	(0.45)

1. The order in which the factors (A to E) are presented is the order obtained for the whole sample and for most subsamples.
2. The order of items within a factor is in descending order of importance for the whole sample. The most frequent item order for the subsamples is also indicated. Items were included until a natural break occurred in the factor loadings around 0.50.
3. Numbers in parenthesis indicate items which appeared in only a few (2–3) subsamples. The position and factor loadings of these items for the whole sample are also given in parenthesis.
4. For one subsample, D was split into two: D1 corresponds to questions 27, 17, 13; D2 corresponds to questions 16, 3, 19.

plausible factors was the standard SPSS-X property that the corresponding eigenvalues of the correlation matrix should be greater than unity. The number of items making an important contribution to the factor was determined by a visual inspection of the plots of the coefficient values corresponding to the item. Items were progressively included until there appeared to be a natural break in the coefficient values, which often occurred at approximately 0.50. All items with values of 0.50 or greater were included.

Large sample

The factor analysis using varimax rotation on the sample of 6000 cases identified six factors with eigenvalues greater than 1. The six factors combined accounted for 50.6% of the variance. We refer to these factors alphabetically in order of decreasing importance. Because the sixth factor contained only a single item (Question 9) which reached our inclusion criterion, details of the factor structure of only the five major factors are presented in Table I. The items contributing significantly to each factor, and the percentage of the variance they account for are presented in Table II.

The oblique rotation resulted in the same five main factors being identified in the same order of importance as in the varimax rotation, except that factor D (as identified by the varimax rotation) accounted for more of the variance than factor C. Table III shows the close similarity in the items which contribute significantly to oblique and varimax rotated factors.

TABLE III

Comparison of items making a significant contribution to varimax rotated factors and oblique rotated factors

Factor	*GHQ items making a significant contribution*							
Varimax A	14	21	28	22	18	15	2	23
Oblique 1	14	21	18	28	22	2	15	23
Varimax B	7	8	4	6				
Oblique 2	7	8	4	6				
Varimax C	29	24	25	26	30			
Oblique 4	29	25	24	26				
Varimax D	16	17	27	13	19			
Oblique 3	17	16	27	13	19			
Varimax E	11	10	5					
Oblique 5	11	10						

This demonstrates that the factors identified by the varimax rotation in this data set are a good summary of the structure of the GHQ, and that imposing orthogonality does not distort the results.

Analysis of random subsamples

Varimax rotation in each of the 10 random subsamples of 600 cases, revealed six significant factors (eigenvalues greater than 1) in each subsample. Factor A was the strongest factor in every subsample and included the same eight items as in the total sample, although in three of the subsamples one or two additional items made a significant contribution. Factors B, C and D were also identifiable in all ten subsamples although in one sample, D was split into two. Factor E was present in nine subsamples. For Factors B, C, D and E there were slight variations in which items contributed significantly to each factor. The order in which the factors emerged (i.e. their strength) differed to some extent from sample to sample. This is depicted in Table IV. For all subsamples, there were only one or two items which made a significant contribution to the sixth factor. The question numbers corresponding to these items are shown in parentheses.

It can be seen that the extent of overall agreement between the 10 subsamples and between the subsamples and the large sample (Table II) inspires confidence that the factors are robust and that the items which constitute each factor are consistent to an acceptable degree.

TABLE IV

Order of factors for each subsample

Subsample	*Order of factors*[1]					
1	A	B	C	E	D1	D2
2	A	C	B	D	E	(9)
3	A	B	C	D	E	(3)
4	A	B	D	C	E	(9)
5	A	C	B	E	D	(4, 5)
6	A	B	D	C	E	(9, 10)
7	A	C	B	D	E	(3)
8	A	C	B	D	E	(9, 10)
9	A	B	D	C	E	(9)
10	A	B	C	D	(9)	(13)

1. Numbers in parentheses are question numbers.

Analysis by age–sex groupings

Principal-components factor analysis followed by a varimax rotation was repeated for each of the 12 age–sex groups. All groups had at least six significant factors; additional factors usually contained only one or two significant items. The data are presented in Table V. Factor A was the strongest factor in each of the 12 groups and contained the same eight items as in the total sample. Although the order in which the other main factors emerged varied to some extent from group to group, all of the factors identified in the large sample and the ten subsamples also appeared in each of the 12 age–sex groups. This suggests that the factors described in Tables I and II are not only robust for the population as a whole but also for individual sections of the population designated by age and sex.

Interpretation of the factors

Deciding what a particular factor means and applying a suitable label is a rather subjective affair. We have attempted to do this in a commonsense fashion, rather than being influenced by theory or diagnostic conventions, since

TABLE V
Order of factors for each age–sex grouping

Sex	*Age*	n	*Order of factors*								
Men	18–24	343	A	C	D2	B	E	(4, 5)	D1	(20)	(1)
	25–34	495	A	C	B	D	E	(9)	(6)	(5)	
	35–44	520	A	C	B	D	E	(3, 5)			
	45–54	403	A	B	C	D	E	(3)			
	55–64	451	A	D2	(4, 5)	C	B	E	D1		
	65+	437	A	B	D	C	E	(3)	(13, 1, 9)		
Women	18–24	406	A	C	B	D	E	(3)	(4, 5)	(9)	
	25–34	688	A	C	E	D	B	(3)			
	35–44	710	A	C	B	E	D	D2			
	45–54	552	A	B	D	C	E	(3)			
	55–64	490	A	B	C	E	(26)	D	(3)		
	65+	505	A	B	C	D	E	(9, 10)	(3)		

our respondents would have used a lay or commonsense interpretation of the questions. The five factors have accordingly been labelled as follows:

Factor A	anxiety, worry and tension
Factor B	feelings of incompetence, low self-esteem
Factor C	depression, hopelessness
Factor D	difficulty in coping, dispirited
Factor E	social dysfunction

The first three items in Factor A (see Table II) were clearly related to feelings of anxiety, worry and tension, and the last four items could also be interpreted as reflecting these feelings. The only item which presented difficulty was the fourth item (Q. 22: "Been feeling unhappy and depressed?"). However, we did not feel justified in labelling this factor anxiety/unhappiness on the basis of a single item. It is noteworthy that this item does not have a significant loading on the depression factor in our study.

The only other factor which presented interpretive difficulties was Factor D, where the items were rather inhomogeneous. It was particularly difficult to accommodate Q. 19: "Been getting scared or panicky for no good reason?" On the whole, however, it was concluded that in a general population sample, this item probably bears little relationship to diagnosable phobias or panic attacks and could be subsumed under difficulty in coping.

Factor scores

Although we have found a great deal of consistency in the underlying factor structure of the GHQ for different age–sex groups, the scores of these groups on individual factors may show different patterns. Figure 1 presents the mean values of the standardised factor scores (overall mean = 0, s.d. = 1) for each age–sex group, calculated on the basis of the orthogonal factor structure of the sample as a whole.

It can be seen that for four factors and the majority of age groups women have higher factor scores than men, reflecting the fact that women tend to obtain higher scores on the GHQ as a whole (e.g. Goldberg, 1972; Huppert *et al*, 1988). However, the advantage of producing individual factor scores is that we can provide a more detailed characterisation of age and sex differences on the GHQ. For example, it can be seen that scores on Factor A decrease with age, while scores on the other four factors increase with age. Factor A also shows the most pronounced sex difference, particularly for the younger age groups, while Factor F shows a reversal of the usual sex-difference, with women obtaining lower scores than men except in the oldest age group.

Discussion

There have been a number of factor analyses carried out on the General Health Questionnaire, mostly using a varimax rotation. Burvill & Knuiman (1983) employed the full 60-item GHQ and examined a community sample of 2044 in Perth, Australia. They identified five factors which were, in order, physical illness, sleep disturbance, social dysfunction, anxiety/dysphoria, and suicidal ideation. Goldberg & Hillier (1978) chose a four-factor solution for the GHQ-60 on a sample of 523 general-practice patients in Manchester. The factors were, in order, somatic symptoms, anxiety/insomnia, social dysfunction, and severe depression.

The shorter 30-item GHQ was derived from the GHQ-60 by excluding symptoms that were commonly present in subjects with entirely physical illness. Thus the GHQ-30 could be regarded as a measure of more purely psychological or psychosocial symptoms. There have been several factor analyses of the GHQ-30 in relatively large community samples. Goldberg *et al* (1976) report data from a sample of 1310 whites and 1310 blacks in the USA. For both groups, the main factor was labelled depression and anxiety, and it accounted for about 21% of the variance. The authors comment that no matter how many factor solutions they examined (up to seven factors) it was not possible to separate anxiety and depression on the GHQ-30. It is interesting to compare their findings with our own results. An examination of the nine items which make up their anxiety/depression factor shows that

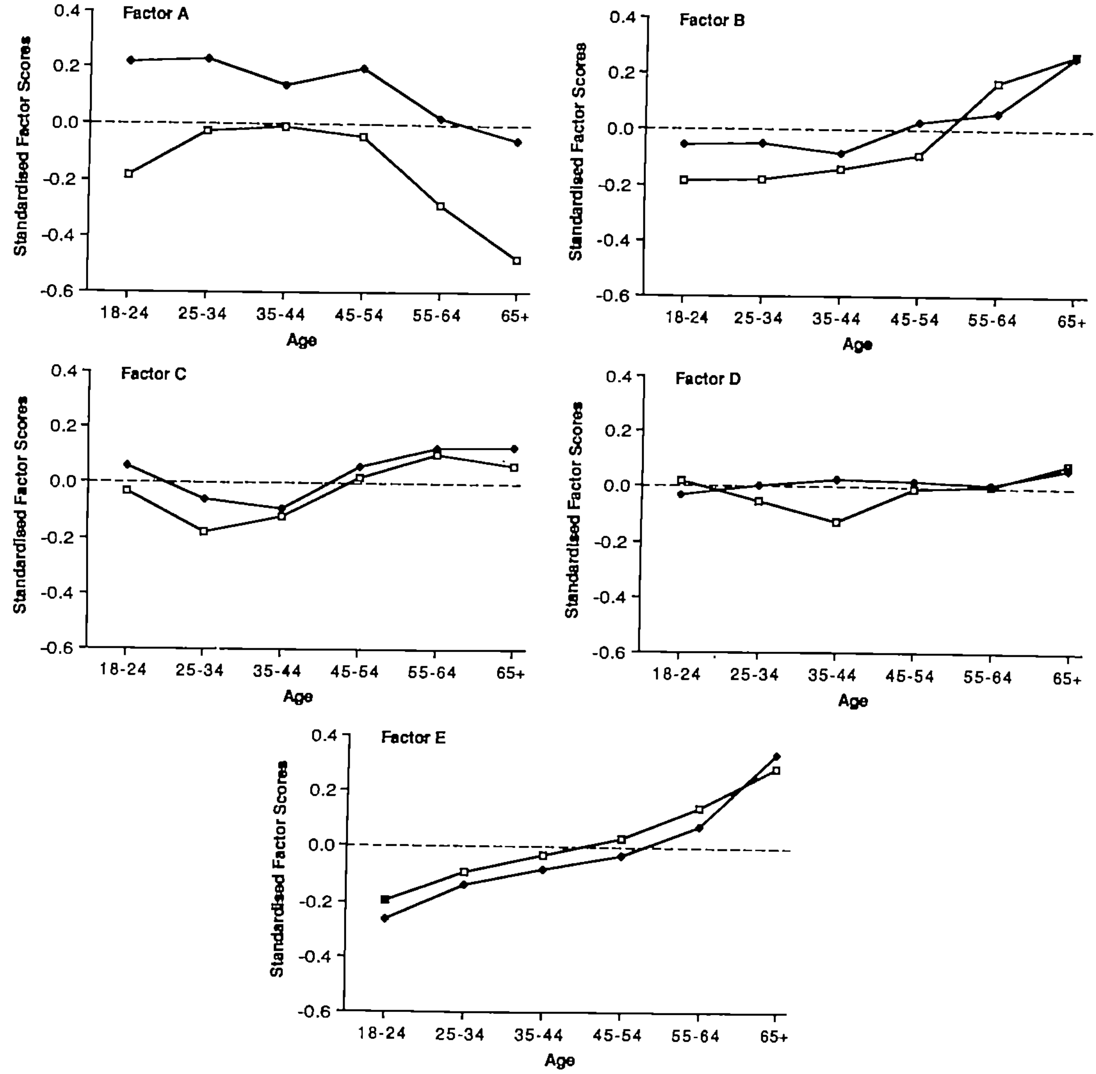

FIG. 1 Standardised factor scores as a function of age and sex (□ male, ■ female).

four items correspond to our anxiety factor, four correspond to our depression factor and one comes from our difficulty-in-coping factor. It is not clear why anxiety and depression were reliably separated in our analyses (and others mentioned below) but not in theirs. This difference is unlikely simply to reflect random fluctuation due to differences in sample size, since our subsamples of 600 are smaller than their samples and yet in each of our 10 subsamples, anxiety and depression emerged as separate factors (Table IV). The possibility of cultural differences in the factor structure or in the interpretation of the items cannot be excluded.

Another factor analysis of the GHQ-30 was undertaken in a community sample of 2000+ in Saskatchewan by D'Arcy (1982). The questionnaire was mailed to respondents and there was a 53% response rate. This raises the possibility that the sample was biased. Indeed, 47% of the sample reported no psychiatric symptoms, compared with only 29% in the Health and Lifestyle Survey, where the response rate was 86.5%. The four factors which D'Arcy identified were anxiety/insomnia, depression/anhedonia, anergia and social dysfunction. The first factor is a combination of our anxiety and difficulty-in-coping factors. Despite the large number of items with significant loadings on D'Arcy's first factor (13 items), it accounts for only 16% of the variance. This contrasts with the eight significant items in our anxiety factor, which accounts for 28.9% of the variance. Five of the nine items in D'Arcy's depression/anhedonia factor clearly correspond to our depression factor, the remaining four not forming part of any coherent factor in our analyses. The anergia factor has no counterpart in our sample, largely because two of the items exist only in the North American version of the GHQ-30. The items which they replace in the original British version have the highest loading on our social dysfunction factor (item 11) and the second highest loading on our feelings-of-incompetence factor (item 8).

Some factor-analytic studies of the GHQ-30 have examined data from highly selected groups. These include the study by D'Arcy & Siddique (1984) on 1038 Canadian adolescents and the study by Chan & Chan (1983) on 255 first-year undergraduates at the Chinese University of Hong Kong. The factor structures which they report are unlikely to be typical of the general adult population, which is the primary focus of this paper. However, it is worth noting that both studies report separate anxiety and depression factors.

None of the previous studies of the GHQ-30 has had a large enough sample size to examine the reliability of the factor structure in a representative population sample. Our study has demonstrated the reliability of a qualitative approach to analysing GHQ data, which yields information not only about the number of symptoms, but also about the nature of these symptoms. We have clearly identified five distinct and robust factors in the GHQ-30. The same factors have emerged in each of the following analyses:

(a) comparing 10 independent random samples of 600 cases each
(b) comparing men and women in each of six age groups from 18 to 98
(c) comparing orthogonal and non-orthogonal factor analyses.

The factors can be labelled anxiety, feelings of incompetence, depression, difficulty in coping, and social dysfunction.

Although age differences are minimal on conventional GHQ scores (e.g. Huppert *et al*, 1987), there are pronounced age differences on most of the factors. Anxiety shows a marked decrease with age, while the other four factors tend to increase with age. Middle-aged adults obtain high anxiety and low depression scores, while older adults obtain high depression and low anxiety scores. Another interesting comparison is between anxiety and feelings of incompetence. Levels of anxiety are very high at age 55–64 in both sexes, and show a marked drop in the age group 65–74. At the same time, feelings of incompetence show a marked rise, particularly in men. A likely explanation for the finding is that leaving paid employment is associated with reduced anxiety, but also with feelings of incompetence or low self-esteem.

The GHQ was developed as a screening instrument for minor psychiatric morbidity: when symptoms are added to yield a score ranging from 0–30 (the GHQ score) the GHQ has been found to have acceptable sensitivity and specificity when validated against clinical diagnosis (e.g. Tarnopolsky *et al*, 1979). We have previously shown that a different scoring method (the CGHQ, which takes account of the chronicity of symptoms) identified different individuals as cases (Huppert *et al*, 1988). The identification of a reliable factor structure for the GHQ-30 raises the possibility that the detection of cases might be improved by examining an individual's profile of scores on the different factors. Further validation studies are required to determine whether the effectiveness of the GHQ as a general psychiatric screening instrument can be improved in this way, and whether the factors relate to specific diagnostic categories.

The GHQ can also be used as a descriptive measure of psychiatric symptoms apart from its use as a screening instrument. The description can be sharpened by the development of empirically derived subscales corresponding to different types of psychiatric symptoms. We have recently derived five subscales based on our factor analysis. We have found that the profile of performance on these subscales varies between groups selected as having a high risk of psychiatric disorder (e.g. the elderly living alone, middle-aged unemployed men). Findings such as these indicate the potential value of GHQ subscales for refining the descriptions of psychiatric symptoms.

Our study, along with most other factor-analytic studies of the GHQ, shows a separation between symptoms of anxiety and symptoms of depression. These studies have been based on community samples, but similar findings have been reported in studies of patients with diagnosed affective disorders. Mullaney (1984) reviewed 40 factor-analytic studies of patients with affective disorders. Although a wide variety of interview schedules was used, all revealed a clear separation between anxiety and depression symptoms. Mullaney concluded that anxiety and depression are separate syndromes. A similar view is implicit in DSM-III-R (American Psychiatric

Association, 1987). There seems little doubt, therefore, that individuals are capable of recognising anxiety symptoms and differentiating them from symptoms of depression or hopelessness. Whether the processes underlying anxiety and depression are different cannot be determined by data of the type we have presented.

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References

AMERICAN PSYCHIATRIC ASSOCIATION (1987) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn, revised). Washington DC: APA.

BLAXTER, M. (1987) Sample and data collection. In *The Health and Lifestyle Survey: Preliminary Report of a Nationwide Survey of the Physical and Mental Health, Attitudes and Lifestyle of a Random Sample of 9003 British Adults* (eds B. D. Cox, M. Blaxter, A. C. J. Buckle *et al*), pp. 1–3. London: Health Promotion Research Trust.

BURVILL, P. W. & KNUIMAN, M. W. (1983) Which version of the General Health Questionnaire should be used in community studies? *Australian and New Zealand Journal of Psychiatry*, **17**, 237–242.

CHAN, D. W. & CHAN, T. S. C. (1983) Reliability, validity and the structure of the General Health Questionnaire in a Chinese context. *Psychological Medicine*, **13**, 363–371.

COX, B. D., BLAXTER, M., BUCKLE, A. C. J. *et al* (1987) *The Health and Lifestyle Survey: Preliminary Report of a Nationwide Survey of the Physical and Mental Health, Attitudes and Lifestyle of a Random Sample of 9003 British Adults.* London: Health Promotion Research Trust.

D'ARCY, C. (1982) Prevalence and correlates of nonpsychotic psychiatric symptoms in the general population. *Canadian Journal of Psychiatry*, **27**, 316–323.

—— & SIDDIQUE, C. M. (1984) Psychological distress among Canadian adolescents. *Psychological Medicine*, **14**, 615–628.

GOLDBERG, D. P. (1972) *The Detection of Psychiatric Illness by Questionnaire.* London: Oxford University Press.

——, RICKELS, K., DOWNING, R. & HESBACHER, P. (1976) A comparison of two psychiatric screening tests. *British Journal of Psychiatry*, **129**, 61–67.

—— & HILLER, V. (1978) A scaled version of the General Health Questionnaire. *Psychological Medicine*, **9**, 139–145.

HUPPERT, F. A., GORE, M. & ROTH, M. (1987) Psychological factors. In *The Health and Lifestyle Survey: Preliminary Report of a Nationwide Survey of the Physical and Mental Health, Attitudes and Lifestyle of a Random Sample of 9003 British Adults* (eds B. D. Cox, M. Blaxter, A. C. J. Buckle *et al*), pp. 51–58. London: Health Promotion Research Trust.

——, —— & ELLIOTT, B. J. (1988) The value of an improved scoring system (CGHQ) for the General Health Questionnaire in a representative British sample. *Psychological Medicine*, **18**, 1001–1006.

MULLANEY, J. A. (1984) The relationship between anxiety and depression: a review of some principal component analytic studies. *Journal of Affective Disorder*, **7**, 139–148.

TARNOPOLSKY, A., HAND, D. J., MCLEAN, E. K. *et al* (1979) Validity and use of a screening questionnaire (GHQ) in the community. *British Journal of Psychiatry*, **134**, 508–515.

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Chronic Psychiatric Complaints and the General Health Questionnaire

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The sensitivity of the GHQ and a revised scoring procedure (CGHQ) for chronic psychiatric complaints was investigated on 175 out-patients. The mean level of severity of symptoms of the groups with and without chronic complaints was not significantly different. However, patients with chronic complaints showed a significantly lower mean GHQ score than patients without chronic complaints. The mean CGHQ scores of the two groups did not differ, suggesting that the CGHQ is a better indicator of the severity of the chronic psychiatric state than the GHQ. The revised scoring procedure resulted in a decrease in the number of false negatives. The strongest reduction in false negatives, however, was induced by a combination of the original and the revised scoring procedures. This reduction was achieved at the expense of only a small increase in the number of false positives. Altogether, the revised scoring procedure proved to be only marginally better.

The General Health Questionnaire (GHQ; Goldberg, 1972, 1978) is a self-report questionnaire directed to the detection of functional psychiatric disorders in the community and primary care settings. In this capacity the instrument has been extensively tested in various cultures and linguistic groups, generally yielding positive results (Harding, 1976; Munoz *et al*, 1978; Henderson *et al*, 1981; Chan & Chan, 1983; Hodiamont, 1986). In addition, there is growing evidence that the GHQ can be used as a measure of severity that fairly accurately reflects changes in the (severity of) psychopathological states (Ormel *et al*, 1989).

Some controversy, however, does exist with regard to the capability of the GHQ as a screening instrument and measure of severity for chronic psychopathology. Various authors have pointed out the relatively large proportion of respondents with chronic complaints that falls within the group of false negatives (Finlay-Jones & Murphy, 1979; Benjamin *et al*, 1982; Hobbs *et al*, 1983; Goodchild & Duncan-Jones, 1985). Other authors, however, report that the chronicity of psychiatric symptoms is, at least in the community, not an important source of misclassification (Goldberg, 1978; Vazquez-Barquero *et al*, 1986).

Goodchild & Duncan-Jones (1985) recently proposed a revised scoring procedure (CGHQ) to eliminate the assumed insensitivity of the GHQ for chronic complaints. They distinguished a subset of items (the so-called negative items) whereby the "no more than usual" answer could possibly indicate the presence of a chronic problem. As contrasted with the conventional scoring procedure the "no more than usual" answers for these items are considered to represent (chronic) pathology and are included in the CGHQ score.

The question whether the revised scoring procedure results in an improvement of the screening capacity of the GHQ has yet to be settled. While Goodchild & Duncan-Jones (1985) reported the CGHQ to be an improvement, Vazquez-Barquero *et al* (1986) could not find any difference in screening capacity between the original and revised scoring procedures. Finally, Sturtees (1987) reported a marginal advantage in favour of the CGHQ, using the advised cut-off point. However, relative operating characteristic (ROC) analysis showed no differences in discriminating power between the GHQ and CGHQ.

The present paper investigates the efficiency of the GHQ-28 as a severity measure and case finding/screening instrument in chronic, as opposed to non-chronic patients, and the assumed superiority of the revised scoring procedure with respect to sensitivity.

Method

Sample

To enhance the possibility of finding answers to the research questions, we selected a population with a high prevalence of psychiatric disorders, including a significant number of chronic cases, even though the GHQ was developed for use in the community and primary care settings.

The subjects were 175 psychiatric out-patients, selected from 460 consecutive referrals to all three psychiatric out-patient clinics of a city (population 175 000) in the north of the Netherlands. From those 460 we excluded psychotic and addicted patients, and those with signs of organic impairment or mental retardation, in total 121. Because of organisational difficulties another 46 patients were not approached. The remaining 293 were asked to participate: 95 (32.4%) refused, 23 (7.8%) dropped out during the course of the study, leaving 175 probands (58% female, mean age 32, s.d. 10).

Design

A semi-structured psychiatric interview was conducted within one to two weeks after the first visit to the clinic. Some days before the interview the GHQ-28 was sent out with the instruction to the respondent to return it at the interview.

The GHQ-28

The GHQ-28 (Goldberg & Hillier, 1979) is a scaled 28-item version of the original GHQ-60. The GHQ-28 was rated in the following ways:

(a) in accordance with the original scoring procedure (Goldberg, 1978): 0011 for all 28 items, a GHQ total score of 5 being the threshold for a psychiatric case
(b) with the revised scoring procedure (Goodchild & Duncan-Jones, 1985): 0111 for the 20 negative items and 0011 for the remaining eight items.

This revised version will henceforth be referred to as the CGHQ. In the absence of a representative sample of non-cases we were not able to establish the optimal threshold score for the revised version. For this reason a CGHQ total score of 13 (the value Goodchild & Duncan-Jones (1985) proposed for the GHQ-30), has been taken as the threshold score for a psychiatric case.

In the present paper we focus on the assumed insensitivity of the GHQ for chronic complaints, and hence we are mainly interested in the false negatives. Although one could argue that the threshold level GHQ ≥5 or CGHQ ≥13 should be raised in a psychiatric (out-patient) population, it would only increase the number of false negatives.

The Present State Examination and DSM-III diagnosis

An extended version of the Present State Examination (PSE) was used to ascertain the existence, severity and nature of present psychopathology. The extended PSE consisted of the original PSE (Wing *et al*, 1974) and a number of additional questions and criteria (regarding eating disorders, somatoform disorders, psychological factors affecting physical condition, adjustment disorders, anxiety syndromes without autonomous symptoms and the duration of long-standing (minor) mood disturbances), that allowed us to assign a DSM-III diagnosis to each patient.

The PSE was conducted by three experienced clinical psychiatrists, a psychiatric epidemiologist and a clinical psychologist, all of whom had extensive PSE training and experience. DSM-III diagnoses (APA, 1980), based on all information systematically collected with the extended PSE, were made for all patients during a consensus-meeting. In approximately one-third of all DSM-III cases multiple axis-I diagnoses were assigned. In these cases a principal diagnosis was given based on an explicit, though arbitrary, hierarchy, which was, however, in accordance with the hierarchic rules and diagnostic strategies of DSM-III. The following hierarchy was adhered to: major depression, somatisation disorder, dysthymic disorder, atypical depression, post-traumatic stress disorder, agoraphobia, panic disorder, simple phobia, social phobia, generalised anxiety, atypical anxiety, psychological factors affecting physical condition, conversion disorders, eating disorders and adjustment disorders.

TABLE I
Duration of complaints at the time of interview

	Frequency	*Relative c.f.*[1]
≥10 years	21	0.12
5–10 years	26	0.27
2–5 years	32	0.45
1–2 years	31	0.63
6–12 months	28	0.79
0–6 months	35	1.00
Total	173[2]	

1. Relative *cumulative* frequency.
2. For two respondents the duration could not be established.

Chronicity of the complaints

During the PSE interview inquiries were made concerning the duration of the complaints prior to referral. Chronic complaints were defined as complaints that, at the time of the interview, had existed for more than 12 months.

Results

Chronicity and prevalence of psychopathology in our sample

Table I shows the duration of complaints at the time of the interview. Of the patients, 63% had complaints which arose more than 12 months prior to referral, and for 27% of the patients this was 5 years or more.

Table II shows the prevalence of psychopathology in our sample. Patients with and without chronic complaints did not differ with respect to caseness. Table II also demonstrates that we succeeded in selecting a sample with high prevalence. For a further description of the sample in terms of psychopathology see van den Brink *et al* (1989).

Influence of chronicity of complaints on the (C)GHQ as a measure of severity

Table III shows the mean (C)GHQ score and mean PSE total score and ID for the groups of patients with and without chronic complaints. Although there were no differences in severity of current symptomatology between

TABLE II
Prevalence of PSE and DSM-III cases in the sample

	Chronic (n = *110)*	*Non-chronic* (n = *63)*	*Total sample* (n = *173)*
PSE-ID ≥5: %	0.69	0.71	0.70
DSM-III cases: %	0.89	0.84	0.87

TABLE III

Mean GHQ, CGHQ, PSE total and PSE–ID scores for respondents with and without chronic complaints

Measure of severity	*Duration of complaints at the time of the interview*				P¹
	Less than 12 months (n = 63)		*More than 12 months* (n = 110)		
	X	*s.d.*	X	*s.d.*	
GHQ	17.27	7.26	14.54	7.94	0.026
CGHQ	21.10	5.26	20.04	5.07	0.192
PSE total score	16.21	9.59	15.26	8.19	0.495
PSE–ID	4.97	1.46	4.88	1.27	0.684

*Probability *T* value (*t*-test independent samples).

TABLE IV

ANCOVA: dependent variable, GHQ score

Source of variation	*Sum of squares (SS)*	*d.f.*	*Mean squares (MS)*	*F*	P¹
Covariate					
PSE–ID	2358.797	1	2358.797	51.108	0.000
Main effect,					
duration	248.377	1	248.377	5.382	0.022
Explained	2607.174	2	1303.587	28.245	0.000
Residual	7845.981	170	46.153		
Total	10453.155	172	60.774		

1. Probability *F*-ratio.

TABLE V

ANCOVA: dependent variable, CGHQ score

Source of variation	*Sum of squares (SS)*	*d.f.*	*Mean squares (MS)*	*F*	P¹
Covariates					
PSE–ID	1104.605	1	1104.605	54.908	0.000
Main effect,					
duration	32.341	1	32.341	1.608	0.207
Explained	1136.946	2	568.473	28.258	0.000
Residual	3419.940	170	20.117		
Total	4556.885	172	26.494		

1. Probability *F*-ratio.

the two groups (the PSE total score and the PSE–ID were not significantly different), the mean GHQ score in the chronic group was significantly lower than in the non-chronic group. The mean score for patients with chronic complaints, however, was still far above the GHQ case criterion. The mean CGHQ score for both groups did not differ.

To estimate the effect of the duration of complaints on the (C)GHQ score, we conducted an analysis of covariance with the (C)GHQ score as the dependent variable, duration as the independent variable and the severity of illness (PSE–ID) as a covariate (Tables IV and V). From these tables the following conclusions can be drawn:

(a) As expected, the largest proportion of the explained variance in the GHQ score has to be ascribed to differences in severity as indicated by PSE–ID

(b) After adjustment for the differences in severity, the duration of the complaints still shows a significant effect on the GHQ (Table IV), but there is no significant effect of duration on the CGHQ (Table V).

Comparable results were obtained when the PSE total score was used instead of the PSE–ID.

Influence of chronicity of complaints on the (C)GHQ as case-finding instrument

The quality of a case-finding instrument is often expressed in terms of misclassification rates, false positives, false negatives, sensitivity, specificity, and positive and negative predictive values. In the present paper we focus on the assumed insensitivity of the GHQ for chronic psychopathology, and hence we are most interested in its sensitivity, and the proportion and characteristics of the false negatives. The design of our study is unsuitable for a prediction of the specificity or false positive rate since we do not have a representative sample of non-cases. However, changes in the overall misclassification rate do give some indication of the effect of the revised scoring method on the false positive rate in this sample.

Tables VI and VII show the sensitivity, the number of false negatives and the overall misclassification rate of the C(GHQ) with PSE–ID ≥ 5 and DSM–III (caseness) as external criteria respectively. The tables contain separate results for the total population and for patients with and without chronic psychiatric complaints.

All respondents were referred to a psychiatric out-patient clinic by their family doctor on account of their complaints. This makes it plausible that the respondents perceived their problems in psychological or psychiatric terms, giving an increased probability of their being a GHQ case. With this in mind we can expect the GHQ to show good sensitivity to both the PSE–ID ≥ 5 and DSM–III. Despite this fact, even in our specific population, the GHQ failed to detect a number of cases. Application of the traditional GHQ scoring procedure in combination with the PSE case criterion resulted in four false negatives, whereas the DSM–III case criterion gave rise to 12 false negatives. The tables show a relation between chronicity and false negatives. All

TABLE VI

Sensitivity and specificity of the GHQ, CGHQ and combined scores to PSE (ID≥5)

	GHQ ≥5	CGHQ ≥13	Combined
Total sample			
No. of false negatives	4	1	0
Sensitivity	0.97	0.99	1.00
Misclassification rate	0.25	0.25	0.26
Chronics			
No. of false negatives	4	0	0
Sensitivity	0.95	1.00	1.00
Misclassification rate	0.25	0.24	0.27
	$P \leq 0.10$	NS	
Non-chronics			
No. of false negatives	0	1	0
Sensitivity	1.00	0.98	1.00
Misclassification rate	0.24	0.25	0.25

PSE false negatives have chronic complaints. The same holds for 11 of the 12 DSM-III false negatives. With DSM-III as criterion, differences in sensitivity between the chronic and non-chronic group were significant ($z=2.56$, $P \leq 0.05$). When the DSM-III diagnoses of the false negatives are taken into account (Table VIII), there is some indication that the GHQ may be less sensitive to chronic anxiety than to chronic affective disorders. Of the four PSE false negatives, three pertain to an anxiety disorder as principal diagnosis and one to an affective disorder. The 12 DSM-III false negatives comprise six anxiety disorders and only one affective disorder.

Application of the revised scoring procedure (CGHQ) results in a decrease in original false negatives, but unfortunately creates several new false negatives (PSE/DSM-III cases with GHQ ≥5 and CGHQ <13). However, the overall reduction of PSE-false negatives is still 75% (leaving only one false negative), and 42% of DSM-III false negatives (leaving seven false negatives). With the CGHQ, the differences in sensitivity to DSM-III between the chronic and non-chronic groups is no longer significant.

TABLE VII

Sensitivity and specificity of the GHQ, CGHQ and combined scores to DSM-III

	GHQ ≥5	CGHQ ≥13	Combined
Total sample			
No. of false negatives	12	7	3
Sensitivity	0.92	0.95	0.98
Misclassification rate	0.16	0.14	0.12
Chronics			
No. of false negatives	11	5	2
Sensitivity	0.89	0.95	0.98
Misclassification rate	0.17	0.13	0.10
	$P \leq 0.05$	NS	
Non-chronics			
No. of false negatives	1	2	1
Sensitivity	0.98	0.96	0.98
Misclassification rate	0.14	0.16	0.16

TABLE VIII

DSM-III diagnosis, GHQ and CGHQ score and duration of complaints of the false negatives (GHQ <5)

Duration and DSM-III diagnosis	*False negatives case criterion*			
	PSE ID≥5[1]	*DSM-III caseness*[2]	*GHQ total score*	*CGHQ total score*
0–6 months:				
Obsessive compulsive disorder (300.30)	–	+	1	9
1–2 years:				
Agoraphobia with panic attacks (300.21)	–	+	4	17
2–5 years:				
Psychological factors affecting physical condition (316.00)	–	+	0	09
Dysthymic disorder (300.40)	+	+	2	20
Social phobia (300.23)	+	+	0	17
Unspecified mental disorder (non-psychotic) (300.90)	–	+	1	13
Psychological factors affecting physical condition (316.00)	–	+	0	13
5–10 years:				
Diagnosis deferred (799.90)	–	+	2	9
Atypical eating disorder (307.50)	–	+	3	15
Agoraphobia with panic attacks (300.21)	+	+	2	21
Panic disorder (300.21)	+	+	2	13
≥10 years:				
Generalised anxiety disorder (300.02)	–	+	0	16

1. + = PSE-ID≥5; – = PSE-ID <5.
2. + = DSM-III caseness.

A combination of both scoring procedures (either GHQ ≥5 or CGHQ ≥13) yields the best results with no PSE false negatives at all and a 75% decrease in DSM-III false negatives (three false negatives left). The decrease in the number of false negatives is achieved at the expense of a slight increase in the number of false positives, resulting in a marginal increase in the overall misclassification rate with the PSE as the external criterion, and a slight decrease in the overall misclassification rate with the DSM-III as the external criterion.

Discussion

Our data demonstrate a relation between GHQ score and the duration of psychiatric complaints.

Patients with chronic complaints had a lower mean GHQ score than the non-chronic patient group, whereas there were no differences in the severity of the actual complaints (as defined by PSE) at the time of the assessment. An analysis of covariance showed a significant relation between duration and the GHQ score. The mean GHQ score for patients with chronic complaints, however, was still far above the GHQ case level. In contrast, the CGHQ score seemed to be insensitive for the duration of complaints. Neither the comparison of patients with and without chronic complaints nor the analysis of covariance showed a significant relation between duration of complaints and CGHQ score.

When using the GHQ as a screening instrument it is important to minimise the number of cases that are not detected by the GHQ (false negatives) (while not gaining too many false positives). Various authors (Finlay-Jones & Murphy, 1979; Benjamin *et al*, 1982; Goodchild & Duncan-Jones, 1985) have suggested that false negatives largely result from the relative insensitivity of the GHQ for chronic disorders. The results of our research corroborates this supposition. With the exception of one patient, all false negatives showed evidence of long-standing psychopathology. The exception concerns a 19-year-old woman with an obsessive–compulsive disorder of less than six months' duration and a masochistic personality disorder. Anxiety disorders comprise more than half the false negatives, whereas affective disorders hardly appear here at all.

In consonance with Surtees (1987) we found that application of the revised scoring method resulted in an increased sensitivity of the GHQ in the chronic group. The best results, however, were obtained by combining the GHQ and CGHQ case criteria. In this event a respondent is considered a case with either a GHQ score ≥5 or a CGHQ score ≥13. The costs in terms of false positives cannot be predicted with our study design. However, there are some indications that these might be low. When DSM–III caseness was used as a criterion, application of the combined GHQ case criterion also resulted in a reduction of the overall misclassification rate. Furthermore, neither Goodchild & Duncan-Jones (1985) nor Surtees (1987) observed a substantial increase in the number of false positives when they used the revised scoring method in community samples.

In sum, the revised scoring procedure seems the better with regard to both the GHQ as a measure of severity and the GHQ as a screening instrument, but the gains appear to be marginal. However, there remains the intriguing finding that all but one of the false negatives are chronics. For conclusive answers more research is needed, with different populations, a range of scoring procedures and different cut-off points.

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References

American Psychiatric Association (1980) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn). Washington, DC: APA.

Benjamin, S., Decalmer, P. & Haran, D. (1982) Community screening for mental illness: a validity study of the General Health Questionnaire. *British Journal of Psychiatry*, **140**, 174–180.

Brink, W., van den Koeter, M. W. J., Ormel, J., *et al* (1989) Psychiatric diagnosis in an outpatient population. A comparative study of PSE-Catego and DSM-III. *Archives of General Psychiatry*, **46**, 369–372.

Chan, D. W. & Chan, T. S. C. (1983) Reliability, validity and the structure of the General Health Questionnaire in a Chinese context. *Psychological Medicine*, **13**, 363–371.

Finlay-Jones, R. A. & Murphy, E. (1979) Severity of psychiatric disorder and the 30-item GHQ. *British Journal of Psychiatry*, **134**, 609–616.

Goldberg, D. (1972) *The Detection of Psychiatric Illness by Questionnaire*, Maudsley monograph no. 21. Oxford: Oxford University Press.

—— (1978) *Manual of the General Health Questionnaire*. Windsor: NFER.

—— & Hillier, V. F. (1979) A scaled version of the General Health Questionnaire. *Psychological Medicine*, **9**, 139–145.

Goodchild, M. E. & Duncan-Jones, P. (1985) Chronicity and the General Health Questionnaire. *British Journal of Psychiatry*, **146**, 55–61.

Harding, T. W. (1976) Validating a method of psychiatric case identification in Jamaica. *Bulletin of the World Health Organization*, **54**, 225–231.

Henderson, S., Byrne, D. G. & Duncan-Jones, P. (1981) *Neurosis and the Social Environment*. New York: Academic Press.

Hobbs, P., Ballinger, C. B. & Smith, A. H. W. (1983) Factor analysis and validation of the General Health Questionnaire in women. *British Journal of Psychiatry*, **142**, 257–264.

Hodiamont, P. P. G. (1986) *Het zoeken van zieke zielen*. Thesis (with English abstract). University of Nijmegen, The Netherlands.

Munoz, P. E., Vazquez-Barquero, J. L., Pastrane, E., *et al* (1978) Study of the validity of Goldberg's 60-item GHQ in its Spanish version. *Social Psychiatry*, **13**, 99–104.

Ormel, J., Koeter, M. W. J., Brink, W., *et al* (1989) Concurrent validity of GHQ-28 and PSE as measures of change. *Psychological Medicine* (in press).

Surtees, P. G. (1987) Psychiatric disorder in the community and the General Health Questionnaire. *British Journal of Psychiatry*, **150**, 828–835.

Varquez-Barquero, J. L., Diez-Manrique, J. F., Pena, C., *et al* (1986) Two-stage design in a community survey. *British Journal of Psychiatry*, **149**, 88–97.

Wing, J. K., Cooper, J. E. & Sartorius, N. (1974) *Measurement and Classification of Psychiatric Symptoms: An Instruction Manual for the PSE and Catego program*. London: Cambridge University Press.

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Differential Classification in School Refusal

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It has been argued that school refusal may not be a unitary syndrome, but a common presenting symptom founded on differing underlying dynamics. The paper explores this hypothesis empirically. The clinical files of 100 refusers were scored for several variables which could potentially differentiate between school refusal subtypes, and for several commonly accepted beliefs about school refusal. The data were subjected to a variety of analyses, culminating in cluster analysis. Cluster (C) 1 consisted of children who feared separation from dependent, overprotective mothers. C2 youngsters were perfectionistic and depressed. They dominated mothers who had been deprived in childhood. C3 consisted of extensively disturbed children from multiproblem families, who had suffered early separation or loss, and who were fearful and depressed.

There is controversy about all aspects of school refusal. Is it a single syndrome with a variety of symptoms, or a variety of syndromes with a common presenting symptom? Atkinson *et al* (1985) presented five parameters which may help distinguish between school refuser types.

(1) *Extensiveness of disturbance* has been dichotomised and labelled neurotic and characterological, or Types 1 and 2, school refusal. Although fearful of school, Type 1 refusers function adequately elsewhere. Type 2 refusers are generally timid, their aversion to school representing one of many fears.
(2) Some refusers experience an acute, others a chronic *mode of onset.*
(3) *Fear source* varies too. Some children are generally fearful, while others are afraid of maternal separation, failure, or the school in general.
(4) *Age* and
(5) *Gender* are also important discriminators (Atkinson *et al*, 1985).

In addition, Kolvin *et al* (1984) divided school refusers into depressed and non-depressed subtypes, although their results were questioned (Atkinson, 1986; Weinberg *et al*, 1986).

The aims of the present study were threefold.

(a) We attempted to determine how the dimensions of differentiation inter-relate.
(b) We explored the adequacy of conclusions drawn on the assumption that the disorder is a unitary syndrome. Several beliefs about school refusers (Table I), derived from four reviews (Atkinson *et al*, 1985; Gordon & Young, 1976; Hersov, 1977; McDonald & Sheppard, 1976), were studied to evaluate how they characterise different types of refusal.
(c) We verified and expanded the profiles with Quay and Parsons' (1971; Quay, 1977, 1979, 1983) Checklist of the Analysis of Life History Data (CALHD), a scale for rating behaviour for three reliable dimensions – psychopathic deviancy, neurotic-disturbed, and subcultural delinquency.

TABLE I
*Commonly cited statements about school refusers as derived from the literature**

Child	
The child: demanding at home; passive at home; outgoing when away from home; manipulative; slept longer than is usual (>1 year) with parents; displays low, average, high intelligence.	
Mother	
The mother: emotionally deprived as child; feels incompetent in maternal role; shows signs of depression; dependent on child for companionship; lacks interests outside family; overprotective; did not desire to become pregnant; is dominant spouse; birth of the patient was feared and/or difficult.	
Father	
The father: dominated by family; peripheral to family affairs; ineffective in dealing with family problems; heavy drinker; emotionally deprived as a child.	
Family Interaction	
Poor marital relations; marriage is intact; mother and child interdependent.	
School	
Teacher perceived as 'mean' (in the American sense); classmates perceived as rough; school work perceived as excessive; academic performance poor; child failed at least one school year; child fears specific aspect of school; child 'acts out' at school.	

*Items which were derived from the literature but which could not be coded for lack of data, or for which reliability ≥0.80 was not reached, were not included in this table.

Method

Data source

Berg *et al* (1969) suggested four diagnostic criteria: (1) severe difficulty in attending school; (2) emotional upset when faced with school; (3) staying at home with parents' knowledge; and (4) absence of significant anti-social disorders. Because in the present study much information was taken from clinical files, where criteria were not easily verifiable, cases were accepted if they met three criteria. All combinations included criterion 1 or 2, ensuring that the *sine qua non* of school refusal, extreme reluctance to attend school, was involved.

Data on 100 refusers were abstracted from the files of four psychiatric facilities. A description of the children was circulated at two facilities and 7 cases were identified in each. At a third institute, perusal of 1250 files, representing all children served in a five-year period, yielded 11 cases. Of the 5735 records examined at the fourth clinic, including all youngsters assessed in a six-year period, 75 cases met the criteria.

The sample includes 61 males and 39 females. Mean age is 11.81 years (s.d. = 3.03 years). The median for years of education was 7, with youngsters having under one year to three years' education falling in the lower quartile, and adolescents with between 10 and 12 years comprising the upper quartile. With regard to diagnostic criteria, (a) extreme difficulty in attending school was explicitly mentioned in 91 cases, (b) emotional upset in 85 cases (all cases met criterion 1 and/or 2), (c) staying at home with parents' knowledge in 81 cases, and an absence of significant antisocial disorders in all cases.

Variables

Eight discriminatory variables were used. With regard to extensiveness of disorder, Kennedy's (1965) Type 1–Type 2 dichotomy presented well-formulated criteria. Kennedy considered any child who met 7 of 10 Type 1 criteria a Type 1 refuser, and likewise for Type 2 refusal (Kennedy, 1965, Table I). In the present study, Kennedy's criterion 4 (education) was eliminated to avoid the artifactual correlation of type and age. Kennedy's criterion 3 (onset mode) could rarely be inferred from the charts, and was dropped altogether.

Kennedy's Type 2 criterion 5 (mother shows neurotic behaviour; father, a character disorder) proved too specific for accurate coding. It was therefore changed to, 'both parents clinically disturbed'. Because parental depression is emphasised in the literature, it was excluded from criterion 5 (and scored separately). Finally, the type dichotomy was made continuous by summing the number of Type 2 criteria that each child met.[1]

Four sources of fear were used. The first was fear of a specific school-related situation (e.g. a rough classmate). Other definitions, based on Smith's (1970) work, were separation anxiety, generalised fearfulness, and extreme perfectionism or fear of failure. Subjects were also classified by age and gender, and according to whether they had been described as depressed. In addition, files were scored for several commonly accepted beliefs about school refusers (Table I) and for the CALHD.

Interjudge reliability was obtained between a blind coder and the first author on 40 files. A further 29 files were scored by the blind judge only, and, for practical reasons, 21 by the first author. Reliability was calculated using Scott's (1955) and Pearson product-moment coefficients. Seven items were discarded for lack of information, and 9 did not reach the 0.80 reliability level; items with reliability ≥ 0.80 were used in further analyses (Table I).

Analyses[2]

Correlation

Pearson correlations (product-moment, point-biserial, phi) were calculated to generate a matrix of discriminatory and literature review variables. Those 12 review items which correlated most highly with at least one discriminatory variable and were statistically significant ($P < 0.05$), were entered into a second matrix with the discriminatory variables. To protect against spurious correlation, the matrix was subjected to the Kaiser–Meyer–Olkin measure of sampling adequacy (MSA) (Kaiser, 1970). Variables which did not meet minimal standards (MSA < 0.50) (Kaiser & Rice, 1974) were dropped from the matrix.

Factor analysis

The final matrix was subjected to principal factoring, varimax rotation, and, to check reliability, unweighted least squares factoring, quartimax rotation. Degree of similarity between factor structures was measured with congruence coefficients (Armenakis *et al*, 1977). Finally, factor scores were calculated for each subject, based on the principal factoring solution.

Cluster analysis

The factor scores were entered into cluster analyses; subjects were classified by both Ward's cluster method with squared Euclidean distances, and the cosine of vectors method with average linkage between groups. Number of clusters was determined with Mojena's (1977) Rule One. To further check reliability, the factor scores were entered into a discriminant analysis and the derived functions were used to predict group membership as originally allocated through cluster analysis.

Inferential statistics

The clusters were then compared across CALHD dimensions using analysis of variance (ANOVA).

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1. The modified Kennedy criteria are available in tabular form from the authors on request.
2. A more detailed description of the analyses and results can be obtained from the authors.

TABLE II

Factor pattern[1] *of discriminant variables and literature review items*

	Factor[2]			
	1	*2*	*3*	*4*
Age	*0.67*	−0.10	−0.03	0.09
Extensiveness	*0.48*	0.24	0.17	−0.15
Child's depression	*0.42*	0.17	*0.45*	−0.22
Separation anxiety	0.12	*0.78*	−0.07	0.14
General fear	*0.70*	0.16	0.00	−0.01
Perfectionism/fear of failure	−0.08	0.12	*0.75*	0.23
Separation/loss	*0.45*	0.10	−0.12	−0.12
Manipulative	−0.04	0.10	0.17	*0.78*
Slept long with parents	−0.07	*0.32*	−0.02	0.11
Intelligence	0.19	0.14	0.10	*0.66*
Failed at least 1 school year	*0.42*	0.05	0.06	*−0.44*
Dominates parents	0.11	0.04	*0.70*	0.07
Maternal incompetence	*0.78*	−0.09	−0.10	0.00
Maternal depression	*0.68*	−0.02	0.18	0.10
Mother deprived	0.08	0.09	*0.39*	−0.13
Overprotective	−0.20	*0.67*	0.20	0.00
Interdependence	0.13	*0.79*	0.05	0.01
% Variance	17.3	12.0	9.4	8.5

1. Principal factoring, varimax rotation.
2. Factor loadings greater than 0.30 are shown in italics.

Results

The final correlation matrix included six discriminatory variables and 11 literature review items. This matrix was factor analysed. Four factors (Table II) met the eigenvalue >1 criterion, and were extracted by both factor methods (congruence coefficients between 0.86 and 0.97).

Factor (F) 1 (general fearfulness, extensiveness of disorder, depression, age, significant separation/loss, school failure, maternal depression, feelings of maternal incompetence) was conceptualised as 'general fearfulness and extensiveness of disorder'. F2 (separation anxiety, maternal overprotection, child slept longer than is usual with parents, mother–child interdependence) represents 'mutual separation anxiety'. F3 (child's perfectionism/fear of failure, depression, domination of mother, and mother's emotional deprivation as a child) reflects 'perfectionism and fear of failure'. F4 (manipulative, failed at least one school year) was labelled 'manipulative'.

When factor scores were entered into the cluster analyses, three clusters met statistical criteria (Mojena, 1977) and were replicated across both cluster methods. Discriminant analyses showed 95% and 99% agreement in subject classification with Ward's and cosine procedures, respectively. Because of its superior reliability in relation to discriminant analysis, the cosine results form the basis of further discussion. C1 consisted of 15 children with separation anxiety (F2). C2 included 28 perfectionistic (F3) youngsters. C3 represented 29 extensively disturbed (F1) children. Twenty-eight individuals remained unclassified.

TABLE III

Mean and standard deviation of CALHD[1] *dimensions for school refusal clusters*

Dimension	*Cluster*					
	1 (Separation anxiety)		*2 (Fear of failure)*		*3 (Extensive disorder)*	
	Mean	*s.d.*	*Mean*	*s.d.*	*Mean*	*s.d.*
Psychopathic deviancy	0.06	1.24	0.64	1.24	1.59	1.64
Subcultural delinquency	−0.73	0.80	−0.29	0.94	−0.52	1.09
Neurotic-disturbed	3.20	1.93	2.25	1.65	3.76	2.39

1. Checklist of the Analysis of Life History Data.

Next, the clusters were compared across the CALHD dimensions. Table III gives the means and standard deviations of the dimensions for the clusters. ANOVA showed significant differences between clusters for psychopathic deviancy ($F(2,71)=3.45$, $P<0.05$) and the neurotic-disturbed dimension ($F(2,71)=3.97$, $P<0.025$). Subsequent contrasts revealed that C3 subjects (extensively disturbed) received significantly higher psychopathic deviancy scores than either C1 (separation anxiety; $F(1,71)=4.17$, $P<0.05$) or C2 participants (perfectionistic; $F(1,71)=5.50$, $P<0.025$). C3 subjects also scored higher than C2 refusers for the neurotic-disturbed dimension ($F(1,71)=7.85$, $P<0.01$). No significant differences emerged for subcultural delinquency ($F(2,71)=0.42$, NS).

Discussion

Extensiveness of disturbance

C3 consisted of 29 Type 2 refusers, as described by Coolidge *et al* (1957), Waldfogel *et al* (1957) and Kennedy (1965). These children scored high on a modified version of Kennedy's (1965) Type 2 scale, which is largely concerned with familial difficulties. Type 2 children were older (mean age 13.9 years; s.d. = 2.23 years). They suffered depression and pervasive fear. Often they experienced academic failure, possibly reflecting intellectual difficulties (Coolidge *et al*, 1957). The mothers were depressed also, and doubted their maternal competence.

Most C3 children (68%) have experienced a separation or loss. The most frequent loss was of the father, either through divorce (18.2%) or death (9%). This is interesting given the Kolvin *et al* (1984) finding that depressed refusers are more likely to live with only one biological parent.

Loss was also experienced through the death of a grandparent (22%). Grandparents are important in the lives of school refusers. Often a parent has not achieved appropriate separation from his or her own parents (Bowlby, 1973; Coolidge *et al*, 1957; Davidson, 1960; Eisenberg, 1958; Estes *et al*, 1956; Johnson *et al*, 1941; Weiss & Cain, 1964).

As well as an extensive form of disorder, investigators have discussed more limited disturbances. These are represented by C1 (reciprocal separation anxiety) and C2 (perfectionism/fear of failure). With their tight groupings of few high loading variables, these clusters suggest circumscribed forms of disorder, as discussed below.

Separation anxiety

The 15 children of C1 showed separation anxiety. They feared leaving an overprotective and dependent mother, with whom they had slept longer than is usual. This dynamic forms the core of psychoanalytic theorising (Atkinson *et al*, 1985).

Perfectionism and fear of failure

The dynamic of perfectionism and fear of failure emerged among the 28 C2 youngsters. The combined occurrence of perfectionism and domination has been mentioned by theorisers of psychoanalytic (Waldfogel *et al*, 1957) and psychodynamic (Radin, 1967) orientation alike. They postulate that it is partly because the child so completely dominates his or her parents, he or she develops an inflated self-concept (Leventhal & Sills, 1964; Millar, 1961; Radin, 1967; Waldfogel *et al*, 1957). When school threatens failure, the child retreats to some area of competence.

The C2 child is depressed. An association between perfectionism and depression in school refusal was also noted by Smith (1970). Perhaps the link is not surprising, given the 'severe narcissistic blow' (Waldfogel *et al*, 1957) to the child's 'fragile sense of self-worth' (Millar, 1961) delivered by academic demands. Radin (1967) posited that the perfectionistic child's depression is rage turned inward.

The mothers of C2 children were emotionally deprived as children. This may be why they have low self-esteem and need to believe in their children's superiority (Radin, 1967).

School refuser types and the CALHD

When clusters were compared across the CALHD dimensions, no differences emerged for subcultural delinquency: all groups scored in the negative range (Table III). One of the criteria for acceptance in this study was an absence of anti-social disorders.

For the neurotic-disturbed dimension, C3 (extensively disturbed) refusers scored significantly higher than C2 (perfectionistic) children. This dimension includes such descriptors as shy, sensitive, submissive, lonely, and anxious.

C3 refusers scored significantly higher than C1 and C2 refusers for psychopathic deviancy. This suggests that C3 children form poor relationships, are more likely to be irritable and to feel persecuted, and are less likely to profit from praise or punishment. Overall, these results again suggest the more extensive nature of C3 disturbance. This reflects well on the discriminant validity of the clusters, at least in terms of C3 against the other groupings.

The immediate concern for future research is replication of the present study to eliminate methodological shortcomings. As is inevitable in case file research, we were unable to judge the reliability of clinical record data; variables which exist in degree had to be rendered dichotomous; variables were excluded from analysis for lack of data; and 28 refusers remained unclassified. However, confirmation of the subclassificatory scheme might permit researchers to tackle the unresolved issues of school refusal with more homogeneous patient groupings.

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References

ARMENAKIS, A., FIELD, H. & WILMOTH, J. (1977) An alogorithm for assessing factor structure congruence. *Educational and Psychological Measurement*, 37, 213–214.

ATKINSON, L. (1986) Depression in school phobia. *British Journal of Psychiatry*, **148**, 335–336.

——, QUARRINGTON, B. & CYR, J. (1985) School refusal: the heterogeneity of a concept. *American Journal of Orthopsychiatry*, **55**, 83–101.

BERG, I., NICHOLS, K. & PRITCHARD, C. (1969) School phobia – its classification and relationship to dependency. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, **10**, 123–141.

BOWLBY, J. (1973) *Attachment and Loss, Volume II. Separation: Anxiety and Anger*. Harmondsworth: Penguin.

COOLIDGE, J., HAHN, P. & PECK, A. (1957) School phobia: neurotic crisis or way of life. *American Journal of Orthopsychiatry*, **27**, 296–306.

DAVIDSON, S. (1960) School phobia as a manifestation of family disturbance: its structure and treatment. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, **1**, 270–287.

EISENBERG, L. (1958) School phobia: a study in the communication of anxiety. *American Journal of Psychiatry*, **114**, 712–718.

ESTES, H., HAYLETT, C. & JOHNSON, E. (1956) Separation anxiety. *American Journal of Psychotherapy*, **10**, 682–695.

Gordon, D. & Young, R. (1976) School phobia: a discussion of aetiology, treatment and evaluation. *Psychological Reports*, **39**, 783–804.

Hersov, L. (1977) School refusal. In *Child Psychiatry: Modern Approaches* (eds M. Rutter and L. Hersov). Oxford: Blackwell.

Johnson, A., Falstein, E., Szurek, S., *et al* (1941) School phobia. *American Journal of Orthopsychiatry*, **11**, 702–711.

Kaiser, H. (1970) A second generation Little Jiffy. *Psychometrika*, **35**, 401–416.

—— & Rice, J. (1974) Little Jiffy, Mark IV. *Educational and Psychological Measurement*, **34**, 111–117.

Kennedy, W. (1965) School phobia: rapid treatment of fifty cases. *Journal of Abnormal Psychology*, **70**, 285–289.

Kolvin, I., Berney, T. & Bhate, S. (1984) Classification and diagnosis of depression in school phobia. *British Journal of Psychiatry*, **145**, 347–357.

Leventhal, T. & Sills, M. (1964) Self-image in school phobia. *American Journal of Orthopsychiatry*, **34**, 685–695.

McDonald, J. & Sheppard, G. (1976) School phobia: an overview. *Journal of School Psychology*, **14**, 291–306.

Millar, T. (1961) The child who refuses to attend school. *American Journal of Psychiatry*, **118**, 398–404.

Mojena, R. (1977) Hierarchical group methods and stopping rules: an evaluation. *The Computer Journal*, **20**, 359–363.

Quay, H. (1977) Measuring dimensions of deviant behaviour: the Behaviour Problem Checklist. *Journal of Abnormal Child Psychology*, **5**, 277–287.

—— (1979) Classification. In *Psychopathological Disorders of Childhood* (eds H. Quay & J. Wherry). Toronto: John Wiley & Sons.

—— (1983) A dimensional approach to behaviour disorder: the Revised Behaviour Problem Checklist. *School Psychology Review*, **12**, 244–249.

—— & Parsons, L. (1971) *The Differential Behavioral Classification of the Juvenile Offender*. West Virginia: Robert F. Kennedy Youth Centre.

Radin, S. (1967) Psychodynamic aspects of school phobia. *Comprehensive Psychiatry*, **8**, 119–128.

Scott, W. (1955) Reliability of content analysis: the case of nominal coding. *Public Opinion Quarterly*, **19**, 321–325.

Smith, S. (1970) School refusal with anxiety: a review of sixty-three cases. *Canadian Psychiatric Association Journal*, **15**, 257–264.

Waldfogel, S., Coolidge, J. & Hahn, P. (1957) The development, meaning and management of school phobia. *American Journal of Orthopsychiatry*, **27**, 754–776.

Weinberg, W., Enslie, G. & Wilkes, C. (1986) Depression in school phobia. *British Journal of Psychiatry*, **148**, 335.

Weiss, M. & Cain, B. (1964) Residential treatment of children and adolescents with school phobia. *American Journal of Orthopsychiatry*, 34, 103–114.

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Distorting Patient or Distorting Instrument?

Body Shape Disturbance in Patients with Anorexia Nervosa and Bulimia

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Three current techniques for estimating body size (Image Marking, Visual Size Estimation, and Distorting Video techniques) were compared. Anorexia nervosa and bulimic patients and normal control subjects were required to make size judgements of the way they 'knew' they looked, the way they 'felt' they looked, and of the width of an inanimate control object. Results from the three techniques were not the same, thus implying that research findings can no longer be cross-compared. Moreover, while all subjects were similar in the accuracy of their estimation of a control object, anorexia nervosa and bulimic patients overestimated their own body size significantly more than normal controls. This difference was even more marked when affective instructions were compared.

The suggestion by Bruch (1962) that a disturbance of body image is characteristic of anorexia nervosa has led to a plethora of reports in the literature endeavouring to quantify patients' perceptions of their own bodies so as to provide empirical evidence for their assumption.

Several objective techniques of body image assessment have been utilised; the most frequently used being a distorting lens or video technique (Garner & Garfinkel, 1981; Freeman *et al*, 1984; Touyz *et al*, 1984*a*) and techniques involving size estimation between two body points (Slade & Russell, 1973; Askevold, 1975).

The results obtained from many of these studies have been inconsistent. While anorexia nervosa patients have been found to significantly overestimate their body shape by some (Slade & Russell, 1973; Pierloot & Houben, 1978), others have found them to be more acute (Ben-Tovim *et al*, 1979). Several studies have found that not only anorexia nervosa patients, but normal-weight subjects as well, overestimate their body shape (Button *et al*, 1977; Ben-Tovim *et al*, 1979). There is now considerable debate as to the extent of overestimation and whether the phenomenon should be considered to be pathognomic of anorexia nervosa. Hsu (1982), after a careful review of the literature, recommended that a disturbance in body image should be deleted as a specific diagnostic criterion for anorexia nervosa. Slade (1985), in his review of techniques developed to assess body shape disturbance, observed that the nature and extent of the deviation appeared to be dependent on the measurement technique used. In a general sense, studies of size-estimation measurement techniques found that most subjects overestimated their body shapes but that anorexia nervosa patients did so more than others. When distorting-image techniques were used, normal subjects were found to underestimate while anorexia nervosa patients tended to overestimate their body shape.

Several recent studies have suggested that bulimics as well as anorexia nervosa patients overestimate their body shape when compared with normal controls (Whitehouse *et al*, 1986; Thompson *et al*, 1986; Touyz *et al*, 1985). Furthermore, bulimics may in fact overestimate their body shape to a greater extent than restricting anorexics (Button *et al*, 1977; Thompson *et al*, 1986). On the other hand, Birtchnell *et al* (1988) found no differences in overestimation tendencies between 50 mixed bulimia nervosa patients and 19 age-matched controls. They also noted that those bulimics with a previous history of anorexia nervosa overestimated their body shape to a lesser degree than those without such a history. Such conflicting data may in fact be the result of different methodologies adopted in the various studies.

Recent attention therefore has focused upon the role of instructions and expectancies in size overestimation. The importance of demand characteristics and instructions was first demonstrated by Crisp & Kalucy (1974), when they challenged their anorexia nervosa patients to "drop their guard" when making their judgements. They found that all patients decreased their overestimations. Using a slightly different approach, Touyz *et al* (1984*b*) attempted to differentiate between cognitive (how subjects 'knew' or 'believed' they looked) and affective (how they 'felt' they looked) judgements. They found that the anorexia nervosa patients perceived themselves quite accurately but felt themselves to be much larger than they actually were. Proctor & Morley (1986) also found much larger estimations for affective or 'internal' instructions than cognitive or 'external' instructions with a group of restricting and bulimic anorexia nervosa patients. Their anorexia nervosa patients also overestimated their body shapes when compared with normal controls for both instructional sets.

The primary aim of the present study was to compare three current measures of body size estimation under controlled experimental conditions using clearly defined groups of eating-disordered patients. Also examined was the way in which the degree of overestimation was influenced by demand characteristics and instructions to attend to particular cues (internal/affective or external/cognitive). To our knowledge, no study has as yet satisfactorily compared the major size-estimation measures and distortion techniques under the same experimental conditions. Thus the extent to which the different techniques may have contributed to the variability of previous research findings remains unknown, as does the contribution of the many other variables known to influence size estimation (e.g. age, weight, and severity of symptomatology).

Method

Subjects

The experimental group comprised 24 female patients (12 anorexia nervosa patients and 12 bulimics) who were consecutively referred to an eating-disorders clinic at a large teaching hospital. Established diagnostic criteria were adopted for both anorexia nervosa (Russell, 1970) and bulimia (DSM-III) (American Psychiatric Association, 1980). Only restricting anorexia nervosa patients were included in the study. All the bulimics, and all but four of the anorexia nervosa patients, were out-patients. None of the bulimic patients had a previous history of anorexia nervosa.

The control subjects ($n = 24$) were all female first-year psychology students who were selected on the basis of having no history of an eating disorder as assessed by the Eating Attitudes Test (EAT) (Garner & Garfinkel, 1979) and the Eating Disorder Inventory (EDI) (Garner & Olmsted, 1983).

Demographic data for all subjects are given in Table I.

TABLE I
Means and standard deviations of age, weight and height of subjects

	Anorexia nervosa (n = 12)		*Bulimics (n = 12)*		*Control subjects (n = 24)*	
	Mean	*s.d.*	*Mean*	*s.d.*	*Mean*	*s.d.*
Age: years	19.4	(4.2)	23.6	(5.6)	19.2	(2.7)
Weight: kg	42.1	(5.7)	59.4	(7.5)	59.4	(7.8)
Height: m	161.0	(5.5)	164.0	(6.4)	166.0	(5.9)

Apparatus and procedure

Body shape perception was measured with three commonly used estimation techniques: the Visual Size Estimation (VSE) apparatus, the Image Marking method, and the Distorting Television/Video method.

All subjects were assessed individually during a single testing session. Total assessment time was approximately 30 minutes for the body size estimation and 15 minutes for the completion of questionnaires.

Three tasks were required on each apparatus. Subjects were asked to make a cognitive and affective appraisal of their body size, and an appraisal of an inanimate object (a box).

Visual Size Estimation apparatus

The VSE apparatus was constructed according to the specification of Slade & Russell (1973): two lights were mounted on a horizontal bar at eye level, and could be moved towards or away from each other by rotation of a handle. The measuring instrument was attached to the bar so that the distance between the lights could be recorded by the experimenter.

The subjects stood 1.55 metres in front of the apparatus. The lights were extinguished and the results were recorded with the aid of a small torch after each estimation was made. Four trials, two ascending (starting at the thin extreme) and two descending (starting at the fat extreme), were conducted on each body part and the results were averaged.

In all, four body parts were assessed (chest, waist, hips, and thighs). A measure of body perception accuracy – the Body Perception Index (BPI) (Slade & Russell, 1973) – was derived for each body width using the following formula: BPI = perceived size/real size) × 100. These results were then averaged to produce a whole-body BPI.

The following instructions were given to each subject.

Cognitive. "I am going to move these lights slowly outwards/inwards; please tell me to stop where you *know* your chest/waist/hip/thighs actually is/are. That is, if you had to measure it/them with a tape measure."

Affective. "I am going to move these lights slowly outwards/inwards; please tell me to stop when the distance between them is equal to where it *feels* like your chest/waist/hips/thighs is/are. That is, where it/they feel(s) like it/they is/are to you."

Control object. "Now hold this box between your hands and tell me to stop when the distance between the lights reaches the width of the box."

One-day test–retest reliability was conducted on this apparatus prior to the commencement of the study. Results for this were consistent with estimates reported by Ben-Tovim & Crisp (1984) ($r = 0.75$–0.79 depending on body part; all significant at $P < 0.001$ level).

Image Marking method

The Image Marking (IM) method simply consisted of a white board and markers (after Askevold, 1975). The subject stood in front of the board and was asked to mark on the board, with a pen in each hand, two points corresponding to the width of each designated body part.

The instructions given to each subject were essentially the same as those described for the VSE technique. One-day test–retest reliability was assessed. Good reliability estimates were obtained for shoulders, hips, and thighs ($r = 0.71–0.85$, $P < 0.01$), but reliability coefficients for chest and waist were poor ($r = 0.38$ for both, $P < 0.001$). One trial was given for each body part, and BPI were calculated for each body part and for the whole body as in the Visual Size Estimation method.

Distorting Television method

The Distorting Television apparatus consisted of a video camera fitted with a zoom lens that scanned a black and white photograph taken with a Polaroid instant camera. The photograph was fixed to a board and scanned by the video camera, and the signal was fed into a television monitor. The image could be varied only in the horizontal plane to give a fatter or thinner figure without distorting height. The apparatus was calibrated so that a control-dial setting of 100 indicated 100% accuracy in the judgement of body width, a setting of 50 an underestimation by 50%, and a setting of 150 an overestimation by 50%. The percentage over- or underestimations could then be compared with the whole-body BPIs of the VSE and IM techniques. One-day test–retest reliability of 0.92 was obtained using this apparatus.

The subject was handed the control dial with the calibrations covered and given the following instructions.

> *Cognitive*. "Please turn the dial until the picture reaches the way you actually *know* you look; as though you had to take a tape measure and actually measure yourself."
>
> *Affective*. "Please turn the dial until the picture reaches where you *feel* you look – that is, where your body feels like it is to you."
>
> *Control object*. "Now turn the dial until the picture matches the size of the box."

Four trials – two ascending and two descending – were conducted for each stimulus condition, and the results were averaged.

Procedure

The order of presentation of the instructions, of the techniques, and of the directions of the trials were counterbalanced to avoid directional effects.

After completion of the body size estimations, the subject's height and weight were recorded. Actual body widths were measured using a body caliper. Then the questionnaires were administered.

Questionnaires

The EAT (Garner & Garfinkel, 1979), EDI (Garner & Olmsted, 1983), and Body Shape Questionnaire (BSQ) (Cooper *et al*, 1987) were administered to all subjects.

Results

A three-way analysis of variance with repeated measures was used to analyse the data. Planned contrasts were used to test for predicted differences.

The bulimic patients were significantly older than the other subjects ($P < 0.01$) but this reflects real clinical characteristics (bulimic patients are typically older than anorexia nervosa patients). The most important consideration was to equate the age of the anorexia nervosa patients with that of the control subjects to avoid the developmental considerations demonstrated by Halmi *et al* (1977). Age did not significantly correlate with any judgement, therefore it was not used as a covariate.

Using the video technique, anorexia and bulimia patients were even more accurate than controls on the cognitive task, but overestimated their body size in the affective task. Using the other two techniques, the anorexic and bulimia patients overestimated on both the cognitive and affective tasks as compared with controls ($t = 4.27$, $P < 0.001$). However, there was no significant difference between the anorexic and bulimia nervosa patients ($t = -0.34$, $P < 0.05$) (Table II).

Comparing the different techniques, estimates on the VSE and IM techniques were greater than those on the

TABLE II
Mean BPIs for anorexics, bulimics, and controls, under three stimulus conditions

Technique	*Stimulus*	*Anorexia nervosa patients*		*Bulimics*		*Control subjects*	
		Mean	*s.d.*	*Mean*	*s.d.*	*Mean*	*s.d.*
Video	Cognitive	97.9	(15.7)	99.9	(13.0)	92.5	(9.3)
Video	Affective	107.6	(20.7)	118.0	(13.7)	93.8	(11.2)
Video	Control	90.3	(11.1)	92.7	(13.7)	93.5	(14.8)
VSE	Cognitive	123.5	(16.8)	118.4	(18.0)	108.9	(14.2)
VSE	Affective	127.3	(22.3)	131.1	(27.8)	109.6	(14.6)
VSE	Control	101.3	(10.2)	95.3	(15.1)	102.0	(14.3)
IM	Cognitive	122.3	(19.4)	118.7	(23.3)	101.2	(10.0)
IM	Affective	129.0	(25.5)	140.3	(43.3)	104.6	(9.3)
IM	Control	104.6	(9.3)	101.4	(11.1)	96.6	(7.8)

TABLE III

Pearson product-moment correlation coefficients for technique, stimulus, and questionnaires

Technique–stimulus	*BSQ*	*EAT*	*EDI (BD[1])*	*EDI (DT[2])*
Video–cognitive	NS	NS	NS	NS
Video–affective	0.55***	0.57***	0.40**	0.49***
VSE–cognitive	NS	NS	0.30*	0.30*
VSE–affective	0.45***	0.41**	0.46***	0.46***
IM–cognitive	0.42**	0.51***	0.27*	0.27*
IM–affective	0.56***	0.59***	0.42**	0.42**

1. Body Dissatisfaction subscale.
2. Drive for Thinness subscale.

*$P<0.05$, **$P<0.01$, ***$P<0.001$.

video ($t=6.53$, $P<0.001$). As predicted, there was no difference between estimates on the former two techniques. There was a significant interaction between subject group and stimulus condition ($F(4, 90)=9.30$, $P<0.001$). Results from the planned contrasts revealed that overestimation occurred only on self-assessment of body size, and not on assessment of the dimensions of a control object ($t=7.95$, $P<0.001$). However, there was a significantly greater overestimation made on affective judgements than on cognitive judgements ($t=4.72$, $P<0.001$).

The results of the correlations between body size measures and responses to questionnaires are shown in Table III. The most substantial correlations were found between the questionnaires (BSQ, EAT, and the Body Dissatisfaction and Drive for Thinness subscales of the EDI).

Discussion

The most significant finding of this study, and one that must be taken into consideration in conducting and evaluating future body estimation research, is that the various techniques for measuring body image are *not comparable*. Thus results obtained using one technique cannot be treated as equivalent in corroborating other techniques or findings, as has previously been the case (Norris, 1984; Freeman *et al*, 1985; Thompson *et al*, 1986; Proctor & Morley, 1986).

As Slade (1985) proposed, it appears that the Visual Size Estimation and Image Marking techniques may, with some exceptions, be grouped together, but must be distinguished from the Distorting Video technique. All subjects demonstrated *consistently* less distortion on the video technique than on the former two. These differences make intuitive sense when one considers the tasks that seem to be involved. In the Visual Size Estimation and Image Marking techniques the subjects are required to form a mental image of themselves (using some tactile visual cues), but in the video technique they are confronted by whole visual images of themselves with which to make judgements.

There was little difference between the estimates of how the control subjects 'felt' they looked and how they 'knew' they looked. However, the eating-disordered subjects not only thought that they were bigger than they actually were, but felt much larger as well. For the bulimic patients, this difference was quite dramatic. They felt they were 18–40% larger than their actual size (depending on techniques).

Bruch (1962) considered a disturbance in body image to be a causal factor in the development of anorexia nervosa. "What is pathognomic of anorexia nervosa", she wrote, "is not the severity of the malnutrition *per se*, but rather the distortion of body image associated with it: the absence of concern about emaciation, even when advanced." More recently DSM–III endorsed this view, listing "a disturbance of body image, e.g., claiming to feel fat even when emaciated" as the second of five necessary diagnostic criteria for anorexia nervosa.

The finding that anorexia nervosa patients overestimated their body size to a greater extent than the control subjects in the present study partially supports such a view. However, three critical points diminish the importance of considering body image disturbance as pathognomic of anorexia nervosa.

Firstly, all bulimic patients in the present study overestimated their body size. Although recent studies (Birtchnell *et al*, 1985; Whitehouse *et al*, 1986) have reported similar findings with normal-weight bulimics, it is possible that their results may have been due to those patients having a previous history of anorexia nervosa. Since the present study selected bulimics on the basis of their having no such history, it appears that an eating-disordered population other than anorexics also evidences body size distortion. Secondly, normal-weight control subjects also overestimated their body shape. Several previous studies have reported similar findings (Crisp & Kalucy, 1974; Button *et al*, 1977); but few, apart from Hsu (1982) and Slade (1985) have considered that such findings could also be due to the techniques used. All subjects tend to overestimate their body shapes in Visual Size Estimation and Image Marking tests. Thirdly, not all anorexia nervosa patients gave cognitive overestimations in the present study. Four anorexia nervosa patients (33%) scored below the mean for the control group in the video tests and two (17%) scored below the mean in both the Visual Size Estimation and Image Marking tests. Thus, the evidence appears to argue against a perceptual distortion of body width being a central element in the diagnosis of anorexia nervosa.

In contrast with the cognitive overestimations, there were marked differences between eating-disordered patients and control subjects on the affective instruction. The body image distortion appears to be most significantly manifested in the affective rather than the perceptual domain. Several factors support this conclusion. For example, Hsu (1982) reported that when the anorexia patient was confronted over a period of time in treatment, she would often admit that she was thin (as Hsu argues, this alone should cast doubt on the validity of a perceptual distortion in anorexia nervosa). Furthermore, a significant relationship between self-report measures of self-esteem and body image distortion has been found by Thompson & Thompson (1986). Similarly, Garner & Garfinkel (1981) found a relationship between self-report of self-esteem and body satisfaction ($r = 0.65$, $P < 0.01$) and between amount of body distortion and body satisfaction ($r = -0.48$, $P < 0.05$). A relationship between distortion and depressed mood (Beck Depression Inventory scores) has also been reported (Freeman *et al*, 1985; Taylor & Cooper, 1986). Several studies (e.g. Touyz & Beumont, 1987; Touyz *et al*, 1985) have also reported that eating-disordered patients desired to be a lot thinner than they were, these results being obtained in Distorting Television/Video testing. It appears, therefore, that eating-disordered subjects' dissatisfaction with their bodies, and the contribution this makes to size overestimation, needs to be more thoroughly investigated.

With regard to shape and size estimation, anorexia nervosa patients and bulimics appear to be very similar. The relationship between anorexia nervosa and bulimia remains a complex issue (Russell, 1979; Garfinkel *et al*, 1980; Touyz & Beumont, 1987; Beumont, 1988). Although two groups are distinguishable by weight, many of the characteristics of anorexia nervosa are also shared by bulimic patients. This study makes this particularly apparent, since similarities were noted despite the separation of subjects into bulimic and anorexic groups without the confounding variable of vomiting and purging anorexics (Beumont *et al*, 1975). Other similarities are also evident. Bulimics, like anorexics, almost invariably have a background of restricted eating – although not necessarily weight loss – usually of long duration (Abraham & Beumont, 1982). Garner *et al* (1985) even suggest that evidence of parental obesity in bulimic groups may indicate that bulimics at normal weight are battling a regulated weight or set-point that is considerably above their aesthetic preferences. It appears that in bulimia restricted eating has given way to an alteration between abstinence and episodes of overeating and vomiting (Touyz & Beumont, 1987). Furthermore, while some bulimics are at normal weight or obese, others are in the anorexic weight range, and in many anorexia nervosa is diagnosed simultaneously.

A theory which does appear to receive some support from this study is one which proposes a relationship between body size overestimation and dimensions of negative self-concept. In this study, the way subjects felt their shape to be appeared to differ quite markedly between eating-disordered patients and control subjects and was related to other self-report measures of eating attitudes and body satisfaction (although the correlations were small). Garfinkel & Garner (1982) suggested that low self-esteem and body dissatisfaction may play a role in misperception of size in eating disorders. It is possible that some normal 'weight-preoccupied' individuals may measure their self-worth in this way as well as anorexia nervosa and bulimic patients. This could explain why some normal subjects also overestimate their body size. On the other hand, the fact that not all anorexia nervosa and bulimic patients overestimated body size in this study must also be accounted for. Perhaps, according to this theory, not all eating-disordered subjects can translate their feelings of dissatisfaction into an estimate of their body size.

The measurement of body image remains a complex issue. This is particularly evident when considering the difficulties inherent in accurately measuring the phenomenon and especially when comparing the data derived from different instruments. The findings of the present study point, firstly, to the non-equivalence of major estimation techniques. This finding appears to have far-reaching implications regarding validation of measurement procedures, diagnosis of eating disorders, and the assessment of treatment outcome. Secondly, the finding that body image distortion is more marked when assessed affectively (i.e. how you feel you look rather than how you actually believe you look) indicates the need for further examination of the relationship between psychological factors such as a negative self-concept and body image distortion. Thirdly, the results obtained in the present study tend to de-emphasise the widely endorsed view that body image distortion is a necessary prerequisite for the diagnosis of anorexia nervosa. This issue, in particular, underscores the importance of clearly defining the role of body image disturbance in the diagnosis and treatment of eating disorders.

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References

Abraham, S. F. & Beumont, P. J. V. (1982) How patients describe bulimia or binge eating. *Psychological Medicine*, **12**, 625–635.

American Psychiatric Association (1980) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn). Washington DC: American Psychiatric Association.

Askevold, F. (1975) Measuring body image. *Psychotherapy and Psychosomatics*, **26**, 71–77.

Ben-Tovim, D. I., Whitehead, J. & Crisp, A. H. (1979) A controlled study of the perception of body width in anorexia nervosa. *Journal of Psychosomatic Research*, **23**, 267–272.

—— & Crisp, A. (1984) The reliability of estimates of body width and their relationship to current measured body size among anorexic and normal subjects. *Psychological Medicine*, **14**, 843–846.

Beumont, P. J. V. (1988) Bulimia: is it an illness entity? *International Journal of Eating Disorders*, **7**, 167–176.

——, George, G. C. W. & Smart, D. E. (1975) "Diets" and "vomiters and purgers" in anorexia nervosa. *Psychological Medicine*, **6**, 617–622.

Birtchnell, S. A., Lacey, J. H. & Harte, A. (1985) Body image distortion in bulimia nervosa. *British Journal of Psychiatry*, **147**, 408–412.

Bruch, H. (1962) Perceptual and conceptual disturbances in anorexia nervosa. *Psychosomatic Medicine*, **24**, 187–194.

Button, E. J., Fransella, F. & Slade, P. D. (1977) A reappraisal of body-perception disturbance in anorexia nervosa. *Psychological Medicine*, **7**, 235–243.

Cooper, P. J., Taylor, M. J., Cooper, Z., *et al* (1987) The development and validation of the body shape questionnaire. *International Journal of Eating Disorders*, **6**, 485–494.

Crisp, A. H. & Kalucy, R. S. (1974) Aspects of the perceptual disorders in anorexia nervosa. *British Journal of Medical Psychology*, **47**, 349–361.

Freeman, R. J., Thomas, C. D., Solyom, L., *et al* (1984) A modified video camera for measuring body image distortion: technical description and reliability. *Psychological Medicine*, **14**, 411–416.

——, Beach, B., Davis, R., *et al* (1985) The prediction of relapse in bulimia nervosa. *Journal of Psychiatric Research*, **19**, 349–353.

Garfinkel, P. E., Moldofsky, H. & Garner, D. M. (1980) The heterogeneity of anorexia nervosa: bulimia as a distinct subgroup. *Archives of General Psychiatry*, **37**, 1036–1040.

—— & Garner, D. (1982) *Anorexia Nervosa: a Multidimensional Perspective*. New York: Brunner/Mazel.

Garner, D. M. & Garfinkel, P. E. (1979) The Eating Attitudes Test: an index of the symptoms of anorexia nervosa. *Psychological Medicine*, **9**, 273–279.

—— & —— (1981) Body image in anorexia nervosa: measurement, theory, and clinical implications. *International Journal of Psychiatry in Medicine*, **11**, 263–284.

—— & Olmsted, M. A. (1983) *The Eating Disorder Inventory Manual*. Odessa, Fl: Psychological Assessment Resources.

——, Garfinkel, P. E. & O'Shaughnessy, M. (1985) The validity of the distinction between bulimia with and without anorexia nervosa. *American Journal of Psychiatry*, **142**, 581–587.

Halmi, K., Casper, R. C., Eckert, E. D., *et al* (1977) Perceptual distortion of body image in adolescent girls: distortion of body image in adolescence. *Psychological Medicine*, **7**, 253–257.

Hsu, L. K. G. (1982) Is there a disturbance in body image in anorexia nervosa? *Journal of Nervous and Mental Disease*, **170**, 305–307.

Norris, D. L. (1984) The effects of mirror confrontation on self-estimation of body dimensions in anorexia nervosa, bulimia and two control groups. *Psychological Medicine*, **14**, 835–842.

Pierloot, R. A. & Houben, M. E. (1978) Estimation of body dimensions in anorexia nervosa. *Psychological Medicine*, **7**, 253–257.

Proctor, L. & Morley, S. (1986) 'Demand characteristics' in size estimation in anorexia nervosa. *British Journal of Psychiatry*, **149**, 113–118.

Russell, G. F. M. (1970) Anorexia nervosa. In *Modern Trends in Psychological Medicine* (ed. J. H. Prior). London: Butterworths.

—— (1979) Bulimia nervosa: an ominous variant of anorexia nervosa. *Psychological Medicine*, **9**, 429–448.

Slade, P. (1985) A review of body-image studies in anorexia nervosa and bulimia nervosa. *Journal of Psychiatric Research*, **19**, 255–266.

—— & Russell, G. F. M. (1973) Awareness of body dimensions in anorexia nervosa: cross-sectional and longitudinal studies. *Psychological Medicine*, **3**, 188–199.

Taylor, H. J. & Cooper, J. (1986) Body size overestimation and depression. *British Journal of Clinical Psychology*, **25**, 153–154.

Thompson, J. K., Berland, N. S. W., Linton, P. G., *et al* (1986) Utilization of a self-adjusting light beam in the objective assessment of body distortion in seven eating disorder groups. *International Journal of Eating Disorders*, **5**, 113–120.

—— & Thompson, C. M. (1986) Body size distortion and self-esteem in asymptomatic normal weight males and females. *International Journal of Eating Disorders*, **5**, 1061–1068.

Touyz, S. W., Beumont, P. J. V., Collins, J. K., *et al* (1984*a*) Body shape perception and its disturbance in anorexia nervosa. *British Journal of Psychiatry*, **144**, 167–171.

——, ——, ——, *et al* (1984*b*) Body image perception and prognosis. *Proceedings of the International Conference on Anorexia Nervosa and Related Disorders, Swansea.*

——, ——, ——, *et al* (1985) Body shape perception in bulimia and anorexia nervosa. *International Journal of Eating Disorders*, **413**, 259–266.

—— & —— (1987) Body image and its disturbance. In *Handbook of Eating Disorders Vol. 1: Anorexia Nervosa and Bulimia* (eds P. J. V. Beumont, G. D. Burrows & R. Casper), pp. 173–189. Amsterdam: Elsevier Science Publishers.

Whitehouse, A. M., Freeman, C. L. & Annandale, A. (1986) Body size estimation in bulimia. *British Journal of Psychiatry*, **149**, 98–103.

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Major Depression in Down's Syndrome

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Five patients with trisomy 21 (Down's syndrome (DS)), referred to us for evaluation of dementia, were instead found to have major depression. All had shown cognitive and behavioural deterioration and this had led to a mistaken diagnosis of Alzheimer's disease in two. We outline and contrast the features of major depression and Alzheimer's disease in DS, and suggest that electroconvulsive therapy is an effective treatment for major depression in DS.

A high prevalence of psychiatric disorder has been described among mentally retarded individuals (Rutter *et al*, 1976, Reid, 1972; McLaren & Bryson, 1987) including those with Down's syndrome (DS) (Menolascino, 1964). The presentations of such disorders may be unusual, making diagnosis difficult (Earl, 1934; Rollin, 1946; Reid, 1972). The majority of the psychiatric disorders described in mentally retarded individuals are probably disorders of behaviour (Phillips & Williams, 1975; Jacobson, 1982) of types that are unusual in other populations (Reid *et al*, 1978), and that are related to the degree of mental retardation (Pollock, 1945; O'Connor & Tizard, 1956; Ross, 1972).

Despite earlier disagreement on the diagnosis of affective disorders (major depression; unipolar and bipolar illness) in moderately and severely mentally retarded individuals (Herskovitz & Plesset, 1941; Winokur, 1974), these disorders have been subsequently described although the presentations may be unusual (Reid, 1972; Reid & Naylor, 1976; Heaton-Ward, 1977; Hasan & Mooney, 1979; Wright, 1982). Estimates of the prevalence of affective disorders in mentally retarded individuals vary (Duncan *et al*, 1936; Pollock, 1945; Penrose, 1962; Payne, 1968; Reid & Naylor, 1976; Reid *et al*, 1978; James & Snaith, 1979), partly because different types of population were studied (Ballinger & Reid, 1977) and also because of the difficulty of diagnosis of mood disorders in these individuals (Reid, 1972); however, most estimates are in the range 1–5% in institutional populations (Wright, 1982). It therefore seems likely that affective disorders occur at least as commonly in mentally retarded populations as in the normal population (James & Snaith, 1979).

Few definite cases of affective disorder have been described in individuals with DS (Roith, 1961; Keegan *et al*, 1974; Sovner & DesNoyers Hurley, 1983), and estimates of prevalence remain unclear through lack of systematic study: it has been suggested that these disorders may (Szymanski & Biederman, 1984) or may not be common (Sovner *et al*, 1985; Hucker, 1985). Recognition and diagnosis of affective and other psychiatric disorders in DS is complicated by the particularly poor verbal skills of this population (Silverstein *et al*, 1982). Diagnosis may therefore rely heavily on behavioural observations and information from carers because of the patient's difficulty in reporting mood and affective experiences (Shapiro & Barrett, 1982).

We show that major depression in DS may present as apparent dementia. This behavioural regression may, however, be misdiagnosed, as it is widely recognised that individuals with DS have a particular vulnerability to Alzheimer's disease: almost all individuals with DS develop the neuropathology of Alzheimer's disease by age 40 and may develop clinical dementia (Malamud, 1972; Wisniewski *et al*, 1985). During a longitudinal study of adults with DS over five years (1983–88) we have encountered individuals who were referred for evaluation of apparent dementia but were instead found to have major depression. We describe and contrast the clinical features of Alzheimer's disease and major depression in DS.

Case reports

Affective disorder

We report five patients who were referred for evaluation of apparent dementia who were instead found to have major depression by DSM–III–R criteria.

Case 1

Over three years this 17-year-old white female had shown a fluctuating but progressive loss of adaptive skills and ability to comprehend directions and perform requests. She appeared not to remember previously familiar procedures and became unable to bath, dress or feed herself. Her speech decreased essentially to muteness and she lost interest in family, friends and usual activities. Her appetite decreased, leading to a 15-pound weight loss; sleep became irregular, with initial insomnia of over two hours; and she became incontinent of faeces and urine. She became fearful of familiar objects, showed inappropriate laughter and crying, and occasionally grasped at apparent visual hallucinations. Her gait became slow and hesitant. On rare occasions she was able to perform skills previously considered lost, such as running downstairs or riding a tricycle.

There was no family history of psychiatric illness except alcoholism in the maternal grandfather. Head CT scan, EEG, thyroid function, serum B12, and red blood cell folate were normal. A diagnosis of Alzheimer's disease had been made.

Treatment with nortriptyline 75 mg daily produced no improvement over four weeks. Electroconvulsive therapy (ECT) was commenced after the patient stopped drinking, and resulted in a marked improvement, particularly after the tenth of 14 treatments: the patient started eating and drinking normally, regained lost weight, continence, adaptive skills, and interest in people and activities, and spoke again in sentences. She was able to return to school. She has remained well for one year.

Case 2

Over two years this 24-year-old white male had shown a deterioration in adaptive and skilled behaviour such that he was no longer able to bath or dress himself, and fed himself only clumsily. He became bradykinetic, with a shuffling gait; apathetic; easily fatigued; socially withdrawn; and neglectful of appearance and hygiene. His speech became slower, softer and less distinct. He often appeared sad, frequently cried, and became increasingly irritable, occasionally striking people. He no longer appeared to remember familiar songs, prayers or procedures. His appetite decreased, leading to a 30-pound weight loss, and he developed initial insomnia of two hours. He became fearful of "spaceships" and of a "storm family", and reported seeing and hearing these. He complained of "a motor" and "sounds or voices" in his head. There was no family history of psychiatric illness. Head CT and MRI scans, thyroid function, serum B12 and red blood cell folate were normal. A diagnosis of Alzheimer's disease had been made.

Out-patient treatment with nortriptyline was discontinued because of urinary retention, without achieving therapeutic blood levels. ECT was commenced, and ten treatments resulted in a marked improvement in all symptoms, such that the patient was able again to perform spontaneously activities of daily living, regain interest and pleasure in activities and people, and recommence work in the family business.

Case 3

This 24-year-old white male had suffered a fluctuating but persistent behavioural deterioration over five years, with exacerbations characterised by loss of adaptive skills, decreased speech, bradykinesia, fearfulness, apathy, social withdrawal, neglect of hygiene, and urinary and faecal incontinence. He appeared to have delusions regarding his left side, preferring not to use or move his left arm or the left side of his mouth, and not tolerating people being on his left side. He appeared to attribute a particular significance to the number 4, and developed manneristic ways of going through doorways and climbing stairs. He developed a preference for wearing black clothes. Loss of appetite led to a 25-pound weight loss. Eating became clumsy and he was no longer able to cut up food adequately. Sleep was disturbed, with initial insomnia of over three hours.

There was no family history of psychiatric illness. Head CT scan, EEG, thyroid function, serum B12 and red blood cell folate were normal.

A six-week trial of amitriptyline 225 mg daily was without benefit. ECT was commenced after the patient stopped drinking. A marked improvement was noted after two treatments, and he received a total of five, with complete resolution of symptoms. He has remained well on therapeutic levels of lithium for two years.

Case 4

This 27-year-old profoundly retarded black female had shown a deterioration in adaptive behaviour and work skills over seven months. She had become mute, apathetic, and socially withdrawn, with drooling, psychomotor retardation, amenorrhoea, and anorexia leading to a 60-pound weight loss.

There was no family history of psychiatric illness. Head CT scan, EEG and thyroid function tests were normal. She was treated with amitriptyline 50 mg daily and made a complete recovery over two months, regaining her premorbid skills, activities, appetite, weight and menses. Amitriptyline was discontinued after one year and she has remained well for over three years.

Case 5

This 38-year-old white male had shown a deterioration of behaviour over one year, with falling performance at his sheltered workshop and on the family farm, and decreased interest in these activities. He had become irritable and slow-moving, and often appeared sad and cried. He was frequently fearful, reported seeing "cats' eyes" and hearing voices coming from under a table, and repeatedly covered up mirrors and windows. He had difficulty sleeping, and complained of daily abdominal pain causing him to scream. He became incontinent of urine.

A family history of alcoholism, major depression, and attempted and completed suicide was noted among several first-degree relatives. Head CT scan, EEG, thyroid function tests, serum B12, and red blood cell folate were normal. Oral cholecystogram and upper GI series were normal.

He was treated as an out-patient with amitriptyline 50 mg daily, and made a complete recovery over three weeks. He has remained well for three years.

Alzheimer's disease

Three patients, two females aged 43 and 48, and a male aged 48, had been referred for evaluation of dementia. All had shown a deterioration in cognitive and adaptive skills over 3–5 years according to their carers. This deterioration was relentlessly progressive and was not episodic. All showed impairment of memory as an early sign; for example, one patient who had for years recited a prayer before meals became progressively less able, and eventually unable, to do so. All showed apraxia; for example, initially losing moderate skills at bowling, organ-playing and dancing, and later losing the ability to dress, use eating utensils, and chew and swallow food. In each case, gait became shuffling and then apractic, initially requiring assistance by carers, but progressing to total inability to walk. Each patient showed progressive agnosia and eventually did not recognise and misnamed family members, and did not recognise familiar surroundings. Each became progressively less interested in surroundings and previous activities and appeared confused by them. They became withdrawn and inactive ("like he's in his own world") and eventually each did little more than sit propped in a chair for long periods, requiring carers to adjust their position. Each patient showed aphasia, progressing for example from loss of skill at using the telephone, to nominal dysphasia and perseveration of responses, and eventually to complete loss of receptive and expressive language. All became incontinent and developed *grand mal* seizures. There was no evidence of a pervasive mood change or alteration of vegetative function in any patient, although they became increasingly irritable and developed catastrophic reactions to minor stressors. None showed persistent and systematised behaviour consistent with responses to hallucinations or delusions.

There was no family history of psychiatric illness or Alzheimer's disease in these patients. CT scans of the head revealed cortical atrophy in each case. Ventricular:brain ratios (VBRs) were measured in two patients, and were significantly higher than in a control population of DS patients without signs of dementia. EEGs in these two patients showed excessive diffuse slow-wave activity. Thyroid function was normal in all cases. Each patient showed diffusely increased muscular tone; hyper-reflexia, with overflow of reflexes to other muscle groups; myoclonic jerks; and emergence of snout and grasp reflexes. Plantar reflexes became extensor.

Discussion

Affective disorders have been previously described in mentally retarded individuals, and the prevalence of these disorders among mentally retarded individuals may be at least as high as in the normal population. Diagnosis of affective disorders can be made in mentally retarded patients from clinical features that are similar to those in patients of normal intelligence, and they respond to standard treatments.

The case histories illustrate that affective disorder in DS may present with severe disturbance of cognitive and vegetative function; that the course of behavioural deterioration may fluctuate; that delusions and hallucinations may be prominent; and that ECT is an effective treatment for this disorder in DS. An apparent dementia syndrome may be a common presentation of depression in these individuals, and extended behavioural observations of the course of the illness are essential to diagnose dementia accurately, such as Alzheimer's disease in DS. Features of Alzheimer's disease in DS that may be useful in this differential diagnosis are of relentlessly progressive deterioration in cognition and adaptive behaviour, with early impairment of memory, lack of altered vegetative function, and emergence of abnormal neurological signs.

We suggest that affective disorder should be considered in the differential diagnosis of apparent dementia in individuals with DS, but particularly in the following: those under age 35; those without clear evidence of memory impairment; those with a fluctuating or episodic course of behavioural regression; those with a pronounced change of affect or vegetative function; and those with prominent delusions or hallucinations. A therapeutic trial of antidepressants or ECT may be warranted in such individuals.

These data support previous reports that severely retarded individuals rarely report depressed mood (Reid, 1972), and that withdrawal, apathy, irritability, increased dependency, and somatic complaints or signs (Szymanski & Biederman, 1984) may be observed instead. Although major depression in Down's syndrome can be diagnosed by DSM-III-R criteria, the frequent inability of these individuals to report their subjective experiences means that certain of the DSM-III-R criteria for major depression are of limited usefulness, and diagnosis rests mainly on observations of activity and vegetative function.

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References

Ballinger, B. R. & Reid, A. H. (1977) Psychiatric disorder in an adult training centre and a hospital for the mentally handicapped. *Psychological Medicine*, 7, 525–528.

Duncan, A. G., Penrose, L. S. & Turnbull, R. C. (1936) A survey of the patients in a large mental hospital. *Journal of Neurological Psychopathology*, 16, 225–238.

Earl, C. J. C. (1934) The primitive catatonic psychoses of idiocy. *British Journal of Medical Psychology*, 14, 3–11.

Hasan, Y. M. K. & Mooney, R. P. (1979) Three cases of manic-depressive illness in mentally retarded adults. *American Journal of Psychiatry*, 136, 1069–1071.

Heaton-Ward, A. (1977) Psychosis in mental handicap. *British Journal of Psychiatry*, 130, 525–533.

Herskovitz, H. H. & Plesset, M. R. (1941) Psychoses in adult mental defectives. *Psychiatric Quarterly*, 15, 574–588.

Hucker, S. J. (1985) Is mania incompatible with Down's syndrome? *British Journal of Psychiatry*, 147, 93.

Jacobson, J. W. (1982) Problem behavior and psychiatric impairment within a developmentally disabled population – I. Behavior frequency. *Applied Research in Mental Retardation*, **3**, 121–139.

James, F. E. & Snaith, R. P. (1979) *Psychiatric Illness and Mental Handicap*. London: Gaskell Press.

Keegan, D. L., Pettigrew, A. & Parker, Z. (1974) Psychosis in Down's syndrome treated with amitriptyline. *Canadian Medical Association Journal*, **110**, 1128–1129.

Malamud, N. (1973) Neuropathology of organic brain syndromes associated with aging. In *Aging and the Brain* (ed. C. M. Gaitz), pp. 63–87. New York: Plenum Press.

McLaren, J. & Bryson, S. E. (1987) Review of recent epidemiological studies of mental retardation: prevalence, associated disorders, and etiology. *American Journal of Mental Retardation*, **92**, 243–254.

Menolascino, F. J. (1964) Psychiatric aspects of mongolism. *American Journal of Mental Deficiency*, **69**, 653–660.

O'Connor, N. & Tizard, J. (1956) *The Social Problem of Mental Deficiency*. Oxford: Pergamon Press.

Payne, R. (1968) The psychotic subnormal. *Journal of Mental Subnormality*, **14**, 25–34.

Penrose, L. S. (1962) *The Biology of Mental Defectives*. New York: Grune and Stratton.

Phillips, I. & Williams, N. (1975) Psychopathology and mental retardation: a study of 100 mentally retarded children: I. Psychopathology. *American Journal of Psychiatry*, **132**, 1265–1271.

Pollock, H. M. (1945) Mental disease among mental defectives. *American Journal of Mental Deficiency*, **49**, 477–480.

Reid, A. H. (1972) Psychosis in adult mental defectives: I. Manic-depressive psychosis. *British Journal of Psychiatry*, **120**, 205–212.

—— & Naylor, G. J. (1976) Short cycle manic depressive psychosis in mental defectives: a clinical and physiological study. *American Journal of Mental Deficiency*, **20**, 67–76.

——, Ballinger, B. R. & Heather, B. B. (1978) Behavioral syndromes identified by cluster analysis in a sample of 100 severely and profoundly retarded adults. *Psychological Medicine*, **8**, 399–412.

Roith, A. I. (1961) Psychotic depression in a mongol. *Journal of Mental Subnormality*, **7**, 45–47.

Rollin, H. R. (1946) Personality in mongolism with special reference to incidence of catatonic psychosis. *American Journal of Mental Deficiency*, **50**, 219–223.

Ross, R. T. (1972) Behavioral correlates of levels of intelligence. *American Journal of Mental Deficiency*, **76**, 545–549.

Rutter, M., Tizard, J., Yule, W., *et al* (1976) Isle of Wight Studies 1964–1974. *Psychological Medicine*, **7**, 313–332.

Shapiro, E. S. & Barrett, R. P. (1982) Behavioral assessment of the mentally retarded. In *Treatment Issues and Innovations in Mental Retardation* (eds J. L. Matson & F. Andrasik). New York: Plenum Press.

Silverstein, A. B., Legutki, G., Friedman, S. L., *et al* (1982) Performance of Down's syndrome individuals on the Stanford-Binet intelligence scale. *American Journal of Mental Deficiency*, **86**, 548–551.

Sovner, R. & DesNoyers Hurley, A. (1983) Do the mentally retarded suffer from affective illness? *Archives of General Psychiatry*, **40**, 61–67.

——, —— & LaBrie, R. (1985) Is mania incompatible with Down's syndrome? *British Journal of Psychiatry*, **146**, 319–320.

Szymanski, L. S. & Biederman, J. (1984) Depression and anorexia nervosa of persons with Down syndrome. *American Journal of Mental Deficiency*, **89**, 246–251.

Winokur, B. (1974) Subnormality and its relation to psychiatry. *Lancet*, *ii*, 270–273.

Wisniewski, K. E., Wisniewski, H. M. & Wen, G. Y. (1985) Occurrence of neuropathological changes and dementia of Alzheimer's disease in Down's syndrome. *Annals of Neurology*, **17**, 278–282.

Wright, E. C. (1982) The presentation of mental illness in mentally retarded adults. *British Journal of Psychiatry*, **141**, 496–502.

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Wilson's Disease: a Prospective Study of Psychopathology in 31 Cases*

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A prospective neuropsychiatric study of 31 consecutive subjects with Wilson's disease is reported. Exploratory factor analysis yielded four factors: neurological, cognitive, hepatic/depressive and psychiatric. Significant associations were found between a 'psychopathic' personality factor and neurological and dysarthria scores. The d' and β coefficients of a signal-detection memory task dissociated: the former correlated only with Mini-Mental State and Benton visuospatial task; and the latter with depressive symptoms. Using discriminant function analysis, there was efficient classification of 'psychopathic' personality by dysarthria, and of individual depressive symptoms by disturbance of gait. Biochemical markers of hepatic dysfunction were significantly associated with certain depressive symptoms. No evidence emerged to support the putative association with schizophrenia-like psychosis.

The occurrence of neuropsychiatric symptoms is well recognised in Wilson's disease (WD) (Dening, 1985; Dening & Berrios, 1989). A retrospective study of 195 cases using reliable, operational criteria (Dening & Berrios, 1989) found that in 51% of these the patient exhibited emotional or behavioural disturbance when first seen at a specialist clinic. Disorders of behaviour and personality were the commonest manifestations, and schizophrenia-like psychoses were rare. Disorders of affect, especially depression, and cognitive function also appeared to be common but such ratings were made with less confidence. It was concluded that prospectively-gathered data would be required for further investigation.

Cognitive studies have often been based on small samples (Bornstein *et al*, 1985; Rosselli *et al*, 1987), or tests of doubtful utility (Scheinberg *et al*, 1968; Gouse, 1975; Tarter *et al*, 1987), or both (Knehr & Bearn, 1956; Hayek *et al*, 1973). A problem in selection of instruments has been failure to allow for impairment of motor performance. This difficulty is apparent in two studies from the Mayo Clinic. The first (Goldstein *et al*, 1968) seemed to identify some mild impairments and slight improvement in test scores after treatment. However, a later study (Davis & Goldstein, 1974), using more extensive and sophisticated testing, found impaired motor function and co-ordination but no deficits in higher mental processes. Medalia *et al* (1988), in the most refined investigation to date, compared 18 neurologically-impaired cases of WD with 12 non-neurological cases and 15 normal controls. Patients with neurological involvement performed worse on tests of verbal learning and semantic memory than either comparison group, although recognition scores were not impaired. The authors concluded that neurological cases have a mild deficit in retrieval.

Affective disorders in WD have received scant systematic attention as no study has employed standardised psychiatric instruments in the examination of a large series of cases.

This paper reports a prospective study, using a battery of neurological, psychiatric and psychological instruments to address the following questions arising from our earlier work.

(a) Are different patterns of psychopathology recognisable in WD by statistical means?
(b) What is the relationship between psychological and other symptoms? (Findings from our retrospective study would predict the existence of a strong relationship between neurological and psychological symptoms, and a lack of correlation between psychopathology and markers of peripheral biochemistry, including copper and caeruloplasmin levels, even in patients previously untreated.)
(c) Can neuropsychiatric measures be used to predict other variables (e.g. outcome, biochemistry, or other clinical variables)?
(d) In particular, can any further light be shed on the nature of cognitive and affective disturbances in WD?

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Method

Selection of subjects

Consecutive patients with unequivocal WD (Dening & Berrios, 1989) attending the Wilson's Disease Clinic at Addenbrooke's Hospital were examined, including both new patients and follow-up attenders. A small number of patients (three or four) were not examined, due to the brevity of their visit. It is unlikely that these omissions generated undue bias.

A relative exclusion criterion was lack of comprehension of English. Several patients were from overseas and were included if their conversational English was reasonably fluent. Those unable to speak English were included only if they were being seen for a clinical indication (i.e. if a psychiatric opinion had been requested on clinical grounds), and if an interpreter was available.

No control group was recruited, for two main reasons: first, difficulty in defining appropriate controls; and, second, the internal structure of the data would allow adequate comparisons to be made. In other words, the sample could be used to provide its own internal controls to test specific hypotheses.

Data collection

A clinical protocol was designed to explore aspects of neurological, psychiatric and psychological functioning. General clinical information and biochemical data were also obtained.

Selection of instruments was influenced by findings from the retrospective study. The original design was to include the Present State Examination (PSE; Wing *et al*, 1974), but it was unsuitable for two reasons: because of its preponderance of psychosis items (extremely uncommon in the series (Dening & Berrios, 1989)) and its relatively inflexible behaviour scales; and for the more practical reason that a place on a recommended training course could not be found at the right time.

Neurological symptomatology was assessed by means of the Webster Parkinson's Disease Rating Scale (Webster, 1968; cited by Marsden & Schachter, 1981) and the North-Western University Disability Scale (NWU; Canter *et al*, 1961). Severity of dysarthria was assessed using the intelligibility subscale of the Frenchay Dysarthria Scale (Enderby, 1983).

Psychiatric symptoms were measured using the Comprehensive Psychopathological Rating Scale (CPRS; Asberg *et al*, 1978), selected for its flexible approach to the rating of behavioural disorders; the 30-item General Health Questionnaire (GHQ; Goldberg, 1972); and the Personality Assessment Schedule (PAS; Tyrer & Alexander, 1985), a reliable instrument for assessing abnormal personality. For the PAS scale, an informant was interviewed where possible, with scoring as directed in the PAS manual.

Tests of neuropsychological function included the Mini-Mental State (MMS; Folstein *et al*, 1975); the Benton visuospatial test (Benton *et al*, 1975), a sensitive indicator of right-hemisphere impairment; the Spot-the-Word Test (Baddeley, unpublished), a recently-developed measure of pre-morbid intelligence; and a memory task based on signal-detection theory (Miller *et al*, 1987). The Signal Detection Memory Test is a refinement of tasks of free recall correcting for subjects' guessing rates. It yields two measures: d', a measure of memory efficiency; and β, the criterion measure, influenced by the decision strategy adopted (which may range from conservative to exaggerated guessing). Values of d' and β were calculated using the method of Hochhaus (1972). The Benton test was administered without the use of a tachistoscope, subsequent work (Benton *et al*, 1978) having demonstrated that the duration of image presentation is not a crucial variable.

Spontaneous blink rates, a measure of central dopamine function (Karson, 1983), were unobtrusively measured while patients sat listening quietly to a tape-recorded passage. Blinking was recorded for a three-minute period, and the mean rate per minute was calculated. Rates recorded by this method correlate highly with blink rates measured electrographically (Karson, 1983).

Overall clinical condition was rated by means of the Global Assessment Scale (GAS; Endicott *et al*, 1976) and level of psychotropic medication by an extended version of Summers' (1978) Drug Risk Number (DRN).

Inter-rater reliability

Limited reliability studies were performed by two raters, TRD and a medical student who had received training in the use of the rating scales. Emphasis was on reliable rating of the psychiatric scales. Cohen's kappa (Spitznagel & Helzer, 1985) was used for dichotomic variables (i.e. presence or absence of symptoms on CPRS and personality traits on PAS).

Data management

All cases were examined by TRD. Information was transferred to an IBM AT personal computer for statistical analysis using the SPSS-PC+ package (SPSS, 1986). Scores from rating scales were either used as global scores or else broken down into subscales on an heuristic basis.

Missing data were managed by clinical completion (Tabachnick & Fidell, 1983). Where the subject was unable to perform the test, a value two standard deviations from the mean in the appropriate direction was given. Variables with more than 10% missing data were excluded from further analysis. Clinical completion of missing data on more than two variables was required in only two cases.

Descriptive statistics were first performed, and a correlational matrix of all variables was constructed using the Pearson product–moment coefficient with correction for multiple correlations. Initial correlations were high between neurological and psychiatric scales. However, these associations were inflated by the presence of some items (e.g. speech disturbance, involuntary movements) in both types of scale.

This difficulty was solved by clinical or statistical means. From the Webster scale single items of clinical importance were extracted such as bradykinesia, tremor and gait disturbance. From the CPRS, 12 items of apparent relevance to depression were selected and added to produce a 'depression score'. The remaining items of the Reported Psychopathology subscale were also added together to produce a 'non-depressive' psychopathology score. The PAS data were subjected to factor analysis. Factor scores for each subject were generated by addition of scores on those variables significantly loading on to the interpreted factors, a recognised procedure, despite limitations (Tabachnick & Fidell, 1983).

The simplified variables thus obtained were assembled into a correlational matrix. To examine the underlying structure of the data, exploratory factor analysis was performed, using the Principal Components method with Varimax rotation. Factors extracted were interpreted if eigenvalues were greater than 1.0, and if the factor contained at least three variables with loadings of 0.4 or more.

Tests for causal associations were carried out. Discriminant function analysis (Wilks' method) was used to test the classificatory power of clinical variables with respect to splitting variables which could readily be dichotomised (e.g. good outcome, GHQ caseness, presence/absence of depressive symptoms, 'psychopathy'). The stepwise method of multiple regression was used to examine continuous variables.

Results

In all, 31 patients were entered in the study. Descriptive statistics are summarised in Tables I and II. Mean biochemical and haematological measures fell within the normal laboratory ranges, except for indices of copper metabolism, which were typical of Wilson's disease (low caeruloplasmin, low total serum copper, elevated urinary copper excretion).

Inter-rater reliability ratings revealed mean values of kappa of 0.73 for CPRS items and 0.83 for PAS items, an acceptable degree of reliability.

A full spectrum of illness was encountered, from patients mute and bedridden to others who had never been symptomatic. Nevertheless, as the majority had been on treatment for some time, the sample was biased in terms of relative good health compared with many others. Among neurological symptoms, dysarthria was the commonest, with only seven subjects attaining the minimum score on the Frenchay scale, consistent with our earlier study (Dening & Berrios, 1989). It is, however, possible that observer sensitivity for dysarthria may be greater than for bradykinesia or rigidity. Quite noticeable was the persistence of relatively minor speech and other deficits, often despite years of therapy; thus presumably the result of permanent damage.

Table I
Demographic information (n = 31)

Age: years	
Mean	27.4
s.d.	7.1
Sex	
Male	12 (39%)
Female	19 (61%)
Origin	
UK	25 (81%)
Overseas	6 (19%)
New cases	
Yes	4 (13%)
No[1]	27 (87%)
Family history of WD	
Yes	15 (48%)
No	16 (52%)

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[1] Mean duration of treatment 9.85 (s.d. 5.9) years.

Table II
Symptomatology

	Mean	*s.d.*	*Range* *Min.*	*Max.*	*Missing data*
Global Assessment Scale	71.1	4.3	15	100	0
Neurological					
Webster	6.8	8.3	0	25	0
NWU	42.3	11.5	3	50	0
Intelligibility of speech	6.6	3.6	3	14	0
Blink rate (per minute)	21.3	16.5	2	67	0
Psychiatric					
CPRS	12.5	8.4	1	33	1
Reported subscale	8.2	5.4	1	22	1
Observed subscale	5.0	5.7	0	26	0
PAS	25.1	13.7	2	62	3
GHQ	4.8	7.6	0	26	1
Cognitive					
Mini-Mental State	27.0	5.8	1	30	0
Benton	26.1	4.4	17	33	3
Spot the Word	21.8	4.8	10	28	3
Signal-detection task, d'	2.64	1.90	0.5	4.38	2
Signal-detection task, β	2.49	2.95	0.09	13.3	2

As the sample was biased in the direction of relative good health, the level of psychopathology identified may have been less than that to be expected in cases of acute illness. Nevertheless, there was again a range of severity from normal to about the level of psychiatric in-patient status. Ten individuals (32%) were GHQ 'cases', with four scores of 20 or more. On personality assessment, 16 subjects of the 28 assessed (57%) were rated as abnormal (rating of 4 or more) on at least one item. The method used to create a Depression subscale from the CPRS can be questioned, but the 12 items employed were similar to those used in other studies of depressive symptoms using this instrument (e.g. Montgomery *et al*, 1978). No psychotic symptoms were observed.

In general, cognitive impairments were not severe. Only four cases scored below the threshold on the Mini-Mental State.

TABLE III

Correlations (n = 31, except for Psychopathy and Neurotic 2, where n = 28)

	Bradykinesia	*Tremor*	*Gait*	*Dysarthria*	*MMS*	*Benton*	*d'*	β	*GHQ*	*Depression*	*Non-depressive psycho-pathology*	*Psychopathy*	*Neurotic 2*	*ALT*
Bradykinesia[1]	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Tremor[1]	0.68**	–	–	–	–	–	–	–	–	–	–	–	–	–
Gait[1]	0.85**	0.67**	–	–	–	–	–	–	–	–	–	–	–	–
Dysarthria[2]	0.84**	0.58**	0.75**	–	–	–	–	–	–	–	–	–	–	–
MMS	−0.47*	−0.19	−0.62**	−0.57**	–	–	–	–	–	–	–	–	–	–
Benton	−0.48*	−0.29	−0.54**	−0.61**	0.57**	–	–	–	–	–	–	–	–	–
d'	−0.25	−0.08	−0.31	−0.32	0.59**	0.71**	–	–	–	–	–	–	–	–
β	0.36	0.14	0.48*	0.28	−0.34	−0.16	−0.25	–	–	–	–	–	–	–
GHQ	0.24	0.18	0.44*	0.27	−0.30	−0.36	−0.02	0.54**	–	–	–	–	–	–
Depression[3]	0.40	0.23	0.52*	0.37	−0.49*	−0.47*	−0.15	0.41	0.80**	–	–	–	–	–
Non-depressive psychopathology[3]	0.64**	0.46*	0.57**	0.45*	0.31	−0.31	−0.04	0.25	0.29	0.47*	–	–	–	–
Psychopathy[4]	0.46*	0.33	0.46*	0.64**	0.12	−0.28	0.21	0.19	0.35	0.32	0.39	–	–	–
Neurotic[4]	0.15	−0.09	0.25	0.12	0.07	−0.14	0.25	0.22	0.58**	0.32	0.45*	0.57**	–	–
ALT	−0.16	−0.06	−0.06	−0.15	0.03	−0.09	0.10	−0.08	0.37	0.50*	−0.05	0.02	−0.02	–
Protein	0.00	−0.08	0.04	0.12	−0.03	−0.13	−0.12	−0.09	−0.23	0.40	−0.10	−0.01	0.02	−0.60**

1. Items from Webster scale.
2. From Frenchay Dysarthria scale.
3. Subscores of CPRS.
4. Factors from PAS.

* $P<0.01$, ** $P<0.001$.

Most scores on the Benton test fell within the normal range. Similarly, the mean value of d', an index of memory efficiency, was higher in this cohort than in the control group used with a similar task in another study (Miller & Lewis, 1977). However, it should be noted that the average age of those normal controls was greater than that of the WD sample. The mean value for β, a measure of willingness to guess, fell midway between the values of the normal controls and the depressed experimental group in the Miller & Lewis study (1.74 and 3.51 respectively).

Age of patients was not significantly related to any other variable except duration of treatment ($P<0.01$). Few differences between the sexes emerged, except that males had higher haemoglobin concentrations ($P<0.02$). A positive family history of WD was associated with less neurological symptomatology ($P<0.001$) but no other significant differences. This finding is in keeping with our earlier study; the explanation being that many cases are identified by screening of asymptomatic family members who are then treated before impairments can develop.

Duration of treatment correlated with low levels of neurological symptoms ($P<0.001$), high platelet counts ($P<0.001$) and low urinary copper output ($P<0.01$). Although psychotropic medication was also recorded, only a minority of patients were on such treatment, and useful comparisons could not be made. Measurement of spontaneous blink rate, a marker for central dopaminergic function, did not prove informative in this study, although reduced blink rate was correlated with bradykinesia and facial immobility, variables associated with a Parkinsonian clinical picture.

Factor analysis of the PAS data yielded four factors. The first factor contained nine traits, including impulsiveness, irresponsibility, aggression and (lack of) conscientiousness, and was labelled as 'psychopathic'. The third factor comprised introspection, callousness and aloofness, and was named 'schizoid'. The second and fourth factors were less readily identifiable, but as each seemed to contain neurotic symptoms, they were labelled 'neurotic 1' and 'neurotic 2'.

Important correlations using the modified variables are shown in Table III. The 'schizoid' factor was not significantly related to any other variable; and the 'neurotic 1' factor exhibited associations with neurological symptoms.

Principal-components analysis of the modified variables yielded four factors: 'neurological', 'cognitive', 'hepatic/depressive', and 'psychiatric' (Table IV).

Discriminant function analysis showed that cases with good outcome (GAS of 70 or more) were classified at the rate of 87% by either Webster or CPRS score. GHQ caseness at the recognised cut-off of 3/4 (Goldberg scoring) was classified at a rate of 84% by two variables – impaired walking (NWU) and serum level of alanine aminotransferase (ALT). 'Psychopathic personality disorder', defined at a threshold score of 9/10 on the psychopathic factor of the PAS, was classified at a rate of 79% by dysarthria alone. Two items from the 'Depressive' subscale of the CPRS, pessimism and sadness, were classified both at a rate of 81% by impaired walking (NWU) and abnormal gait (Webster), respectively. Abnormal serum values of ALT (Addenbrooke's normal range: females 0–25 IU/l; males 0–38 IU/l) were classified at a rate of 81% by the variables inability to feel, reduced sleep, and fatigue.

Using regression analysis, impaired walking accounted for 39.9% of the variance in the depression score derived from the CPRS, and for 32.7% of the variance in scores on the Benton visuospatial test. Dysarthria and psychopathic personality together accounted for 43.2% of variance in Mini-Mental State scores; and sadness for 26.2% of that in β (criterion measure of signal detection test). No neurological or psychiatric variable predicted d' to any significant extent.

TABLE IV
Factor analysis of prospective sample

Factor	*Eigenvalue*	*% variance*	*Variables*	*Loadings*
1. Neurological	3.56	27.4	Tremor	0.868
			Gait	0.837
			Frenchay Dysarthria score	0.764
			'Psychopathic' factor	0.675
2. Cognitive	2.63	20.2	Mini-Mental State	0.853
			d'	0.827
			Benton	0.826
			Frenchay Dysarthria score	0.510
3. Hepatic/depressive	1.96	15.1	Serum ALT	0.912
			Serum protein	−0.804
			Depression score	0.744
			GHQ	0.474
4. Psychiatric	1.36	10.5	'Neurotic 2' factor	0.843
			GHQ	0.649
			β	0.582
			Depression score	0.441

Discussion

This series of 31 cases of WD is the largest to have been studied by means of standardised neuropsychiatric instruments in conjunction with biochemical and other data. A recent study of cognition in WD (Medalia *et al*, 1988) involved, coincidentally, the same number of cases as ours. However, this and other studies have neglected other psychopathology, or have used crude qualitative ratings of neurological variables. Furthermore, most of the patients in our study received treatment over a period of time from the same physician, making possible a reliable longitudinal analysis of a large cohort of WD (Dening & Berrios, in preparation).

The series is not typical. There is, firstly, an excess of female subjects, unusual for WD, where a small excess of males is usually found (although the reason is unclear). This may simply indicate that females are more prepared to be followed up. Secondly, a majority of patients had received chelating agents for a considerable time, with several effects: (a) relatively high mean age; (b) relative lack of acute, in particular hepatic, symptoms or biochemical disturbance; (c) bias towards chronic, neurological symptoms or else towards a symptom-free state. Overall, patients in the sample were not severely ill: mean GAS was over 70, corresponding to "minimal symptoms . . . but no more than slight impairment in functioning" (Endicott *et al*, 1976). Caution must therefore be exercised in extending the results of this survey to the entire population of cases of WD. On the other hand, the sample, a consecutive series of attenders, was typical of the proportion of new and follow-up cases which might be seen by a specialist clinic, carrying a full range of symptoms (and variance).

A problem in using batteries of instruments is that items may overlap, leading to inflated correlations. For example, dysarthria was rated on the Webster, NWU and CPRS scales, as well as by the Frenchay scale. Other motor symptoms were also recorded on more than one scale. By the same token the GAS, derived from clinical symptomatology, proved of limited value. As mentioned above, various methods were used to eliminate redundancy. Four neurological variables were retained, each representing a component of the disease picture: bradykinesia, tremor, gait disturbance (ataxia) and dysarthria. Psychiatric items were divided according to the hypothesis that some would reflect affective pathology. Personality data were subjected to a more formal division, by factor analysis, since there was also interest in making comparisons with other studies.

The number of variables examined is relatively large in proportion to the sample size, and the statistical techniques employed may be at the limits of their power. Some findings must therefore be treated with caution. Nonetheless, the main results appear clinically relevant, and some replicate earlier findings from retrospective data.

Neurological symptomatology

The neurological symptoms were highly intercorrelated, but different symptoms were associated in different ways with other manifestations. For example, tremor was not related to psychopathology or cognition, bradykinesia was closely associated with psychopathy, and gait disorder was related to depression and cognition and to abnormal personality. Such a dissociation lends support to previous statistical evidence for neurological heterogeneity in WD (Dening & Berrios, submitted).

Although individual items from the Webster scale were used to seek dissociations in symptomatology, the possibility remains that even individual symptoms, such as dysarthria or rigidity, are not unitary phenomena but are themselves composite variables influenced by lesions at different sites. The relationship of lesions of basal ganglia, cortex and brainstem to peripheral symptoms and signs is not necessarily specific or 'one-to-one'. Thus correlations between neurological symptoms and signs may well be artificially inflated by the varying contributions of different lesions and pathological mechanisms.

Cognitive function

It might be argued that cognitive impairments in this sample, being generally mild, are of limited significance and that cognitive testing has simply separated subjects according to their innate intellectual ability. The finding that scores on a range of tests were highly correlated with each other and less strongly with other variables (with the exception of dysarthria) is consistent with this suggestion. However, when test scores were corrected for pre-morbid intelligence by means of Spot-the-Word test scores, there was no correlation between cognitive and neurological or psychiatric variables.

From these observations it is concluded that there is not a simple relationship between cognition and neuropsychiatric symptomatology. Importantly, some patients who appear obtunded have good cognitive function; for example, one of the highest scores for d' was attained by a drooling, immobile young man with virtual anarthria. Potential associations between disease correlates of cognitive impairment may have been diluted by the small number of patients with such deficits. It is also possible that the cognitive instruments were insufficiently sensitive or specific to demonstrate subtle defects. These uncertainties require further research on a larger, more severely-affected population, or, alternatively, longitudinal studies of newly-diagnosed patients.

The signal-detection criterion measure, β, correlated strongly with measures of depression but not with other cognitive tests. The dissociation of d' and β is well recognised, as is the relationship of β to depression (Miller & Lewis, 1977). Higher β in depressed subjects may reflect a conservative guessing strategy.

Psychiatric symptoms and personality

In the factor analysis of the PAS scores of the 28 cases for whom the schedule was completed, it could be argued that too many variables were used for the number of cases. However, the factor structure obtained was not dissimilar to that described by Tyrer & Alexander (1979).

There are conceptual problems in examining personality characteristics in patients with brain disease, especially if such subjects are relatively young at onset of illness. Also, personality inventories seem to be influenced by mental state (Griffiths, 1970). To some extent this can be circumvented by use of an informant, but, if the illness is chronic, mental state still intrudes. That this process has operated in this study is suggested by the associations between the neurotic 2 personality factor and measures of depressive symptoms.

Probably the most important finding of this study is the prospective replication of our earlier conclusion that disorders of behaviour and personality are significantly related to neurological symptoms, especially dysarthria, bradykinesia and rigidity. These were strong correlations between the psychopathic personality factor, non-depressive psychopathology on CPRS and these neurological measures. In addition, psychopathy and neurology loaded on to the same factor. Dysarthria was the most powerful single predictor of psychopathy when discriminant function analysis was applied. It is evident that the psychopathology of WD is not homogeneous, since syndromes with different correlates can be identified. The data regarding personality and behavioural abnormalities are strongly suggestive of an organic basis for these disorders. Certainly a 'reactive' hypothesis fails to explain why such disorders are associated with some neurological symptoms and not with others (e.g. tremor).

The data also suggest a relationship between metabolic disorder, presumably due to hepatic dysfunction, and depressive symptoms. Serum levels of ALT and protein were correlated significantly with the depression score of the CPRS, and in particular with inability to feel, reduced sleep and loss of interest in sex. Correlations with GHQ score were also positive but just short of statistical significance (e.g. ALT and GHQ: $r=0.37$). On factor analysis, these biochemical variables loaded on to the same factor as GHQ and depression score. With discriminant function analysis, ALT proved one of the most powerful predictors of GHQ 'caseness'. However, it would appear that much of the variance of depressive symptomatology was not explained by hepatic disease, as a second depressive factor was extracted, which also contained the neurotic 2 personality factor and the β criterion measure from the Signal Detection Memory Test, neither of which were at all correlated with hepatic disorder. Correlations were also found between depression and some of the neurological items, although such associations were less striking than those between personality and neurological variables.

Statistical evidence of a contribution by hepatic disease to depression in WD is a new finding, but it should be interpreted with caution, as only three or four patients had significant active hepatic disease; with just one patient, on the verge of liver failure, having severe hepatic symptoms. It is also possible that the biochemical markers used as evidence of hepatic dysfunction were of limited validity.

The mechanism relating depression and hepatic disease is unclear: there may be a simple connection between having a metabolic disorder and feeling unwell, there may be a 'reactive' depression to the seriousness of the disease, or there may be a more complex process whereby depression leads to metabolic abnormality through non-compliance with therapy or some other intervening variable. Perhaps what has been labelled as depression is wrongly named, and should be thought of as 'malaise' or 'weariness' (i.e. it is a behavioural phenocopy of depression).

Nevertheless, the relationship of indices of hepatic disease and symptoms commonly recognised in depression is an important and robust finding. The failure of the retrospective study to indicate this relationship may be due to two factors. Firstly, the threshold for recognition of depression in that study may have been high, with failure to identify milder cases. In addition, clinical and biochemical evaluations may have been performed at different points in time, resulting in a desynchronisation of depressive and hepatic features. In this prospective study, clinical and biochemical testing were simultaneous.

No psychotic symptoms were seen in this study. Our previous work has supported other authors sceptical of a relationship between WD and schizophrenia-like psychoses (e.g. Beard, 1959).

In summary, different patterns of psychopathology can be recognised statistically in WD, and certain changes in mental state appear to reflect organic changes. Characteristic alterations in personality and conduct are probably related to neurological disease; and certain depressive symptoms are associated with hepatic disease and biochemical abnormalities. Cognitive deficits were uncommon and their relationship to neurological disease remains obscure. It has been shown that neuropsychiatric measures can be used to predict other clinical variables, including outcome.

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References

Asberg, M., Perris, C., Schalling, D., *et al* (1978) The CPRS – development and applications of a psychiatric rating scale. *Acta Psychiatrica Scandinavica* (suppl. 271).

Beard, A. W. (1959) The association of hepatolenticular degeneration with schizophrenia. *Acta Psychiatrica Neurologica Scandinavica*, **34**, 411–428.

Benton, A. L., Hannay, H. J. & Varney, N. R. (1975) Visual perception of line direction in patients with unilateral brain disease. *Neurology*, **25**, 907–910.

——, Varney, N. R. & Hamsher, K. (1978) Visuospatial judgement: a clinical test. *Archives of Neurology*, **35**, 364–367.

Bornstein, R. A., McLean, D. R. & Ho, K. (1985) Neuropsychological and electrophysiological examination of a patient with Wilson's disease. *International Journal of Neuroscience*, **26**, 239–247.

Canter, C. J., de la Torre, R. & Mier, M. (1961) A method of evaluating disability in patients with Parkinson's disease. *Journal of Nervous and Mental Disease*, **133**, 143–147.

Davis, L. J. & Goldstein, N. P. (1974) Psychologic investigation of Wilson's disease. *Mayo Clinic Proceedings*, **49**, 409–411.

Dening, T. R. (1985) Psychiatric aspects of Wilson's disease. *British Journal of Psychiatry*, **147**, 677–682.

—— & Berrios, G. E. (1989) Wilson's disease: psychiatric symptomatology in 195 cases. *Archives of General Psychiatry* (in press).

Enderby, P. (1983) *Frenchay Dysarthria Assessment*. Windsor: NFER-Nelson.

Endicott, J., Spitzer, R. L., Fleiss, J. L., *et al* (1976) The Global Assessment Scale: a procedure for measuring overall severity of psychiatric disturbance. *Archives of General Psychiatry*, **33**, 766–771.

Folstein, M. F., Folstein, S. E. & McHugh, P. R. (1975) 'Mini-Mental State': a practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, **12**, 189–198.

Goldberg, D. P. (1972) *The Detection of Psychiatric Illness by Questionnaire*. London: Oxford University Press.

Goldstein, N. P., Ewert, J. C., Randall, R. V., *et al* (1968) Psychiatric aspects of Wilson's disease (hepatolenticular degeneration): results of psychometric tests during long-term therapy. *American Journal of Psychiatry*, **124**, 113–119.

Gouse, A. T. (1975) MD thesis. Yale University.

Griffiths, R. D. (1970) Personality assessment. In *The Psychological Assessment of Mental and Physical Handicap* (ed. P. Mittler). London: Methuen.

Hayek, H. W., Knoll, E. & Widhalm, S. (1973) Über das organische Psychosyndrom bei Morbus Wilson. *Monatsschrift Kinderheilkunde*, **121**, 679–683.

Hochhaus, L. (1972) A table for the calculation of *d'* and *β*. *Psychological Bulletin*, **77**, 375–376.

Karson, C. N. (1983) Spontaneous eye-blink rates and dopaminergic systems. *Brain*, **106**, 643–653.

Knehr, C. A. & Bearn, A. G. (1956) Psychological impairment in Wilson's disease. *Journal of Nervous and Mental Disease*, **124**, 251–255.

Marsden, C. D. & Schachter, M. (1981) Assessment of extrapyramidal disorders. *British Journal of Clinical Pharmacology*, **11**, 129–151.

Medalia, A., Isaacs-Glaberman, K. & Scheinberg, I. H. (1988) Neuropsychological impairment in Wilson's disease. *Archives of Neurology*, **45**, 502–504.

Miller, E. & Lewis, P. (1977) Recognition memory in elderly patients with depression and dementia: a signal detection analysis. *Journal of Abnormal Psychology*, **86**, 84–86.

——, Berrios, G. E. & Politynska, B. (1987) The adverse effect of benzhexol on memory in Parkinson's disease. *Acta Neurologica Scandinavica*, **76**, 278–282.

Montgomery, S., Asberg, M., Jörnestedt, L., *et al* (1978) Reliability of the CPRS between the disciplines of psychiatry, general practice, nursing and psychology in depressed patients. *Acta Psychiatrica Scandinavica*, (suppl. 271), 29–32.

Rosselli, M., Lorenzana, P., Rosselli, A., *et al* (1987) Wilson's disease: a reversible dementia: case report. *Journal of Clinical and Experimental Neuropsychology*, **9**, 399–406.

Scheinberg, I. H., Sternlieb, I. & Richman, J. (1968) Psychiatric manifestations in patients with Wilson's disease. In *Wilson's Disease* (ed. D. Bergsma). *Birth Defects Original Articles Series*, Vol. 4, No. 2. New York: The National Foundation.

Spitznagel, E. L. & Helzer, J. E. (1985) A proposed solution to the base rate problem in the kappa statistic. *Archives of General Psychiatry*, **42**, 725–728.

SPSS Inc. (1986) *SPSS-PC+*. Chicago: SPSS.

Summers, W. K. (1978) A clinical method of estimating drug-induced delirium. *Life Sciences*, **22**, 1511–1516.

Tabachnick, B. G. & Fidell, L. S. (1983) *Using Multivariate Statistics*. New York: Harper & Row.

Tarter, R. E., Switala, J., Carra, J., *et al* (1987) Neuropsychological impairment associated with hepatolenticular degeneration (Wilson's disease) in the absence of overt encephalopathy. *International Journal of Neuroscience*, **37**, 67–71.

Tyrer, P. & Alexander, J. (1979) Classification of personality disorder. *British Journal of Psychiatry*, **135**, 163–167.

—— & —— (1985) *Revised Classification of Personality Using the Personality Assessment Schedule*. Nottingham: Mapperly Hospital.

Webster, D. D. (1968) Clinical analysis of the disability in Parkinson's disease. *Modern Treatment*, **5**, 257–282.

Wing, J. K., Cooper, J. E. & Sartorius, N. (1974) *The Measurement and Classification of Psychiatric Symptoms*. Cambridge: Cambridge University Press.

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An Epidemiological Study of Dementia in a Rural Population of Elderly Women

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A study of 365 women aged 70–79 in a rural community was carried out using the Cambridge Examination of Mental Disorders in the Elderly (CAMDEX). Prevalence rates of dementia are reported by severity for the 70–74 and 75–79 age groups. Differential diagnosis was made according to CAMDEX guidelines. Senile dementia of Alzheimer type accounted for half the dementia cases. The prevalence rates overall did not differ from those reported in other recent studies, but the rates for levels greater than mild/moderate were lower, despite the inclusion of subjects in institutions.

Few studies of dementia and cognitive impairment in the community have been conducted in rural settings in Britain, although comparisons of urban and rural populations have been made in other countries. In Japan, Shibayama *et al* (1986) examined a rural area as part of a larger epidemiological study and found higher rates of dementia in the rural area than in the urban area (2.5% v. 1.5% for severe dementia and 3.8% v. 3.1% for mild dementia). Jorm *et al* (1988), in a review of the literature, found only three surveys of purely rural communities, all of which reported lower rates of dementia than did surveys of the urban elderly (Nielsen, 1962; Jensen, 1963; Akesson, 1969).

Recent studies in Britain have concentrated on urban environments. Morgan *et al* (1987) found a prevalence of 3.2% for cognitive impairment in Nottingham, and Copeland *et al* (1987) reported a prevalence of 5.2% for dementia in Liverpool in the age group over 65. In marked contrast to this, Clarke *et al* (1984) found a prevalence of 1.6% for cognitive impairment in the market town of Melton Mowbray. However, both the Melton Mowbray study and the Nottingham study used a very short scale as the measure of cognitive function. This was the Information/Orientation subscale of the Clifton Assessment Procedures for the Elderly (Pattie & Gilleard, 1979). A cut-off point of 7/8 was used in both studies. The Liverpool study used the Geriatric Mental State (Copeland *et al*, 1976), arriving at a diagnosis using the computerised algorithm AGECAT. No informant interview was included in the AGECAT algorithm at the time and there was little information on cognitive function. Broe *et al* (1976) reported an overall prevalence of 8.1% for dementia in the over-65 age group in a study which included a proportion of rural residents. A marked increase in the prevalence of dementia or cognitive impairment with age was reported in all these studies. The only other rural study has been that of Griffiths *et al* (1987), who examined 100 people aged over 65 from an Oxfordshire village. The sample, however, was made up of healthy volunteers.

The main aim of the study described in this paper was to examine a complete rural population, limited by age and sex, for variables associated with dementia and cognitive impairment.

Method

Subjects and instruments

The study was conducted in a rural area of East Cambridgeshire (part of the Fens). This area was chosen for its population stability and the opportunity to sample from a geographically delimited population. It is relatively unaffected by the flux of the academic population of Cambridge and by London commuter traffic, while not being as isolated as other parts of the Fens. The area, which included one small town and four villages, was served by a single health centre with six general practitioners. There was virtually no cross-boundary flow to other practices in neighbouring areas. There were approximately 11 000 people registered with the practice. A computerised age–sex register was kept continuously up to date.

Because a study of this size conducted on both sexes over an unlimited age range would have produced small numbers in some age groups, and consequently little confidence in the distributions, the age range 70–79 was chosen. Most studies indicate markedly different rates of dementia and cognitive impairment between the under-75s and the over-75s.

The sample consisted of women aged between 70 and 79 on 1 October 1985. All those registered with the health centre, whether in institutions or not, were included, since the study aimed to examine the entire cross-section of the population. Two balanced strata were chosen from the age groups 70–74 and 75–79: the entire older group was included (207 women), and 203 women were randomly selected from the younger group of 270. Ten subjects died before the interviewer was able to see them, leaving

200 potential subjects in each stratum. The study was introduced to each subject by a letter from her own general practitioner. In order to establish if many individuals had been lost to the study because of long-term institutionalisation, a search of the local facilities was carried out at the end of the survey.

The subjects were interviewed where they lived. The interview consisted mainly of the Cambridge Examination of Mental Disorders in the Elderly (CAMDEX; Roth *et al*, 1986, 1988). This is a standardised psychiatric interview designed for use in the elderly, particularly in the early identification of dementia. It comprises

(a) a standardised psychiatric interview with the subject
(b) a mini-neuropsychological battery with the subject (CAMCOG; Roth *et al*, 1988), covering most aspects of cognitive function, with the Mini-Mental State Examination (MMSE; Folstein *et al*, 1975) included
(c) standardised observations of present mental state
(d) a structured interview with an informant
(e) a brief physical examination, and information on medication
(f) some laboratory investigation (in this study venepuncture was performed).

Clinical diagnosis, including differential diagnosis of dementia, was made after informant interview according to guidelines laid down in CAMDEX. In the early version of CAMDEX that was used in the study, the severity gradings for depression and dementia differ from those in the present version: the categories were mild, mild/moderate, moderate, moderate/severe, and severe; and mild incorporated what is now classified as minimal in CAMDEX severity grading. The diagnosis was made without calculation of scores on the cognitive or other scales and without reference to general practitioners' notes.

Additional information was requested, including fuller assessment of social engagement and past medical history. Socioeconomic group was allocated according to the Registrar General's method. The husband's social class was coded where the subject was married or widowed, and the subject's own occupation was coded where she had not been married.

In addition to CAMCOG and MMSE, the Information/Orientation subscale of the Clifton Assessment Procedures for the Elderly (CAPE; Pattie & Gilleard, 1979) was administered. The full interview covered all the items suggested by the Medical Research Council Working Group on Alzheimer's Disease (1987).

Procedure

A small pilot study in an adjoining town with a different health centre was carried out to train the interviewer (CB) and to assess the acceptability of the full interview in the community.

Data collection was then carried out between October 1985 and October 1986. Most of the interviews were conducted in the first seven months. Subjects were interviewed in random order, with the age groups balanced. The subjects were interviewed on their own, as were the informants, since the presence of a third person such as a spouse or other relative could have influenced responses. An informant was requested on all subjects, and, as a result of the pilot study, wherever possible informants were aged under 70 (not part of the study, and less likely to deny change). On average the subject interview, including physical examination and venepuncture, took 90 minutes, and the informant interview 20 minutes.

Quality control

Within two weeks of the initial interview, a random 10% of the sample were re-interviewed by a different interviewer (PC), using the Geriatric Mental State Examination (GMS) – hospital version. These results are presented elsewhere (Brayne & Calloway, unpublished). The completed interview records were checked manually twice before data entry. Full verification of data entry was carried out, and 10% of the entries were checked against the original interview schedules for accuracy.

Results

Details of the sample are given in Table I. After the whole sample had been approached once, all those who had not been seen were approached again in person. Fifteen women agreed to take part at this stage. The final response rate of the available sample, excluding those who died before being interviewed, was 91%. All but four individuals from the available sample were seen. The search of local institutions for individuals of the correct age and area identified only two individuals not known to the study. One of these, who died during the study, had been given a tentative diagnosis of multi-infarct dementia.

There was no difference in social class according to age group: 44% and 45% of the younger and older groups respectively were in social class III, with 23% and 22% in social class IV; 17% of each group were in social class II, and just over 2% in social class I. Those in social class II and IV were mainly associated with agricultural occupations. Many women had also worked on the land themselves.

TABLE I
The sample

	Age group 70–74	*Age group 75–79*
Target sample	272	212
Losses before study began	2	5
Effective sample	270	207
Sample selected	203[1]	207
Deaths during study	3	7
Available sample	200	200
Not seen	2	2
Seen briefly	6	14
Partial interview	7	4
Full interview	185 (92.5%)	180 (90%)

[1] Random.

TABLE II
Prevalence of organic brain syndrome by level of severity (CAMDEX clinical diagnosis)

	Age group 70–74		*Age group 75–79*	
	Number	*Percentage of population*	*Number*	*Percentage of population*
Minimal/mild	8	4.3	16	8.9
Mild+	0	0	5	2.8
	8	4.3	21	11.7

Most of the women lived in independent accommodation, either with their spouse or on their own. Only two lived in long-stay hospitals, and two in residential homes. Fourteen per cent of the older group and 5% of the younger group lived in sheltered accommodation. More women in the younger group were married than widowed (53% and 42% respectively), whereas more women in the older group were widowed than married (58% and 36% respectively). Few were single or divorced.

Educational level was similar for the two groups. In the younger group 79% and in the older group 73% left school at the statutory leaving age of 13/14 – although more of the older group (22%) than the younger group (4%) left school at 13. More of the older group (7%) than the younger group (3%) went on to some kind of further education.

Consent was given by 95.6% (349) of the sample for an informant to be approached. The age range of the informants was 22–77, with only nine aged above 70. The majority (70%) were women. Most (78%) had known the subject for many years, 13% had known the subject for several years and a small proportion (5%) had known the subject for a short period only. Most informants (64%) were children of the subjects, 19% were other close family members, 6% were friends, and the remaining 11% were a miscellaneous group. Most of the informant interviews (76%) were conducted by telephone.

Table II gives the prevalence rates of dementia for the two age groups, using CAMDEX guidelines. Both the minimal/mild category and the mild/moderate and more severe category are more prevalent in the older group than in the younger one. Table III sets out the differential diagnosis for the age groups, again using CAMDEX guidelines. A large difference is seen between the age groups for senile dementia of Alzheimer type (SDAT), but not for multi-infarct dementia (MID). Only one woman was felt to fulfil the criteria for the mixed condition of SDAT and MID. The women with dementia secondary to other causes accounted for a small number and were all graded as mildly affected. One woman, although not fulfilling the criteria for even minimal dementia, was performing under her normal level, secondary to gross hypothyroidism. No women were felt to fulfil the criteria necessary for the diagnosis of acute confusional state at the time of being seen. One woman had suffered from an acute confusional state shortly before being seen, and one woman whose family refused the interview was in a terminal confusional state. One further woman's informant reported recent mild changes in personality and memory: on cognitive testing, minimal patchy cognitive impairment was found, but these changes were not sufficient to fulfil any diagnosis. This individual was found to be markedly hyperglycaemic.

Application of the cut-off point suggested by Roth *et al* (1986) for CAMCOG (79/80) gave a sensitivity of 93% and a specificity of 75% for all dementias, including the minimal/mild category. A cut-off point of 69/70 provided a sensitivity of 86% and specificity of 92%. Excluding the minimal/mild category altered the sensitivity and specificity to 100% and 63% respectively for the 79/80 cut-off point and 100% and 87% respectively for the 69/70 cut-off point.

The total MMSE score can be computed using two methods. In addition to the rest of the items, either the score on serial sevens alone could be included, or the best score on spelling WORLD backwards and serial sevens (each with a possible total of 5). In this female population, this change in scoring shifts the total distribution and affects the cut-off points. When scoring using serial sevens only and

TABLE III
Differential diagnosis of dementia: CAMDEX clinical diagnoses

	Age group 70–74			*Age group 75–79*		
	Number	*Percentage of population*	*Percentage of demented subjects*	*Number*	*Percentage of population*	*Percentage of demented subjects*
SDAT[1]	3	1.6	37.5	12	6.7	57
MID[2]	4	2.2	50	5	2.8	24
SDAT and MID	0	0	0	1	0.6	5
Other	1	0.6	12.5	3	1.6	14
Acute confusion	0	0	0	0	0	0
Total	8	4.3	100	21	11.7	100

1. Senile dementia of Alzheimer type.
2. Multi-infarct dementia.

identifying all demented groups, including minimal/mild, the best cut-off point for the MMSE was 21/22, giving a sensitivity of 83% and a specificity of 87%. This Information/Orientation subscale of CAPE, using a cut-off point of 7/8, could not identify the group of subjects with minimal/mild dementia, but provided a sensitivity of 80% and specificity of 99% when this group was excluded.

No subject in the younger age group scored less than 8 on the Information/Orientation subscale of CAPE, in comparison with 3.3% of the older age group.

Discussion

It was possible to compare these prevalence rates with those found in recent large studies in the UK where age-specific rates were reported. Copeland *et al* (1987), using the computerised algorithm AGECAT, found rates of dementia in women of 4.1% for the 70–74 age group ($n = 194$) and 8.5% for the 75–79 age group ($n = 142$). In Nottingham, Morgan *et al* (1987) found rates of cognitive impairment of 2.1% in the 65–74 age group and 7.2% in the 75+ age group. The rates of 4.3% for the 70–74 age group and 11.7% for the 75–79 age group in the present study were higher, but included mild cases. The figures here include individuals in whom the diagnosis was tentative, even with informant history, and in whom follow-up would be necessary to confirm diagnosis. However, the rates for mild/moderate and severe dementia in the present study were low. Jorm *et al* (1988) found that in prevalence studies where mild categories were included there was a tendency to report lower rates for moderate and severe levels of dementia than in studies in which there was no mild category. The present study appears to conform to this pattern.

As might be expected in this age group, there were few severely affected individuals, and these were found in institutions. High rates of cognitive impairment have been reported in institutional settings, and it is possible that there are different patterns for institutionalisation between rural and urban areas. A lower rate of institutionalisation might be expected in the older age groups in this area because of the greater likelihood of extended support networks, as reflected by the availability of informants.

Jorm *et al* (1988) performed a meta-analysis of the prevalence studies of dementia from 1945 to 1985. The results indicated that the prevalence rates of dementia doubled for each increase in age of 5.1 years. On the basis of this, Jorm *et al* suggested that it was possible to examine a limited age group in detail and to estimate prevalence rates in other age groups from the results. They also found that the age-specific rates for all dementias did not differ significantly between men and women. The rates for the present study could therefore be used to estimate dementia rates for the entire population aged over 70 in this rural population.

If this were done it would give considerably lower prevalence rates for moderate and severe dementia than the estimated rates reported in the meta-analysis of Jorm *et al* (2.8% for the 70–74 age group and 5.6% for the 75–79 age group). However, the rates found in the present study were similar to those found in Scandinavian rural areas for the over-65 age range: Nielsen (1962), Jensen (1963) and Akesson (1969) reported rates of 3.1%, 1.1% and 1.3% respectively.

Differential diagnosis in those in whom an organic brain syndrome was diagnosed has been attempted in this study. In the community setting, without detailed investigation, this is imprecise. It does appear likely that most of the dementia in this sample was due to SDAT, with a markedly higher prevalence in the older age group. The proportion of those in whom MID was diagnosed was similar in the two age groups. If this finding does reflect the underlying neuropathology, the lack of increase of MID with age may be due to the different length of survival of subjects with MID and SDAT in the community. The number of individuals with temporary impairment secondary to known conditions allowing a diagnosis of acute confusional state was very small. It is possible that this group would be larger in older samples, where chronic illness is more prevalent. Secondary dementias formed a small proportion of the total and affected similar numbers in each age group.

Of the 75–79 age group, 3.3% fell below the cut-off point suggested for the Information/Orientation subscale of CAPE. This figure lies in between those found for Melton Mowbray and Nottingham for both sexes aged over 75 (1.6% and 5.6% respectively). However, 40 subjects in the Melton Mowbray sample were not classified, and could have fallen into the impaired category, bringing the percentage up to a maximum of 5.4%. This would be higher than the percentage in the current study, as expected with a sample where there is no upper age limit (only 56% of the Melton Mowbray sample were in the 75–79 age group). The Melton Mowbray results also excluded those subjects who were in hospital or in homes for the elderly; these, if included, would have increased the proportion of impaired people found.

Moreover, women seem to score less well on the Information/Orientation subscale than men. Using the same cut-off point, the Nottingham study, which also examined community residents, identified 2.1% of women in the 65–74 age group and 7.2% of women in the 75+ age group. Only about 2% of men in each age group were identified. This difference may be due to differential survival between the sexes of the cognitively impaired. Male sex and cognitive impairment are both risk factors for shortened survival (Jagger & Clarke, 1988), thus ensuring a lower prevalence of cognitively impaired males in survivors. A further reason could be different patterns of institutionalisation. Taking these differences into account, it seems likely that the populations of Melton Mowbray and the Fens scored similarly, with fewer individuals falling below the cut-off point than in the Nottingham sample.

If the CAMDEX clinical diagnosis is used as a standard, CAMCOG is the most sensitive of the cognitive scales in identifying mild dementia, including minimal cases. MMSE, although considerably shorter, also performs well. The Information/Orientation subscale of CAPE could not identify individuals with minimal/mild dementia in the population studied, but performed well in identifying the mild/moderate and severe cases. In the context of low prevalence, however, the above scales would still have relatively low positive predictive values.

In studies of the elderly, the aims should determine the choice of scale used. If it is necessary to identify mild/moderate and more severe dementia, a short scale such as the Information/Orientation subscale of CAPE is appropriate. For minimal to mild dementia, however, CAMCOG is the most sensitive instrument, but will identify a high proportion of false positives (depending on the cut-off point chosen). MMSE performs at a level in between these two, and where brevity is essential it may be the instrument of choice. The important association of sociodemographic variables such as social class and education with CAMCOG and MMSE is discussed elsewhere (Brayne & Calloway, 1989).

In summary, therefore, in the present study of women aged 70–79 in a rural community, the prevalence estimates for dementia, including the minimal/mild category, were similar to those found in comparable urban samples. However, it is important to note that in a community sample the distinctions between 'normal ageing', minimal and mild dementia are blurred. A dimensional approach would seem to be more appropriate for epidemiological studies of dementia sampling from the whole range of the population, allowing for the possibility of an underlying continuous distribution of the latent variable dementia or SDAT (Brayne & Calloway, 1988). The prevalence estimates for dementia excluding the minimal/mild category were extremely low, and were not accounted for by loss of subjects into institutions. Even with use of a simple scale, such as the Information/Orientation subscale of CAPE, comparison of results is difficult unless exactly the same methodologies are employed. Future studies should account for these points and also for differences in survival, migration patterns and rates of institutionalisation before valid comparisons can be made and aetiological hypotheses tested.

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References

Akesson, H. O. (1969) A population study of senile and arteriosclerotic psychoses. *Human Heredity*, **19**, 546–566.

Brayne, C. & Calloway, P. (1988) Normal ageing, cognitive impairment and Senile Dementia of the Alzheimer's Type – a continuum? *Lancet*, *i*, 1265–1267.

—— & —— (1989) The association of education and socioeconomic status with a measure of the cognitive function of elderly people. *Age and Ageing* (in press).

Broe, G. A., Akhtar, A. J., Andrews, G. R., *et al* (1976) Neurological disorders in the elderly at home. *Journal of Neurology, Neurosurgery and Psychiatry*, **39**, 361–366.

Clarke, M., Clarke, S., Odell, A., *et al* (1984) The elderly at home: health and social status. *Health Trends*, **16**, 3–7.

Copeland, J. R. M., Kelleher, J. M., Kellet, J. M., *et al* (1976) A semi-structured clinical interview for the assessment of diagnosis and mental state in the elderly: the Geriatric Mental State Schedule. I. Development and reliability. *Psychological Medicine*, **6**, 439–449.

——, Dewey, M. E., Wood, N., *et al* (1987) Range of mental illness among the elderly in the community: prevalence in Liverpool using the GMS–AGECAT package. *British Journal of Psychiatry*, **150**, 815–823.

Folstein, M. F., Folstein, S. E. & McHugh, P. R. (1975) Mini-Mental State: a practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, **12**, 189–198.

Griffiths, R. A., Good, W. R., Watson, N. P., *et al* (1987) Depression, dementia and disability in the elderly. *British Journal of Psychiatry*, **150**, 482–493.

Jagger, C. & Clarke, M. (1988) Mortality risks in the elderly: five year follow-up of a total population. *International Journal of Epidemiology*, **17**, 111–114.

Jensen, K. (1963) Psychiatric problems in four Danish old age homes. *Acta Psychiatrica Scandinavica* (suppl. 169), 411–419.

Jorm, A. J., Korten, A. E. & Henderson, A. S. (1988) The prevalence of dementia: a quantitative integration of the literature. *Acta Psychiatrica Scandinavica*, **76**, 465–479.

Medical Research Council Working Group on Alzheimer's Disease (1987) *Report from the MRC Alzheimer's Disease Workshop*. London: MRC.

Morgan, K., Dalloso, H. M., Arie, T., *et al* (1987) Mental health and psychological well-being among the old and the very old living at home. *British Journal of Psychiatry*, **150**, 801–807.

NIELSEN, J. (1962) Geronto-psychiatric period-prevalence investigation in a geographically delimited population. *Acta Psychiatrica Scandinavica*, **38**, 307–330.

PATTIE, A. H. & GILLEARD, C. J. (1979) *Manual of the Clifton Assessment Procedures for the Elderly (CAPE)*. Sevenoaks: Hodder and Stoughton Educational.

ROTH, M., TYM, E., MOUNTJOY, C. Q., *et al* (1986) CAMDEX: a standardised instrument for the diagnosis of mental disorder of the elderly with special reference to the early detection of dementia. *British Journal of Psychiatry*, **149**, 698–708.

——, HUPPERT, F. A., TYM, E., *et al* (1988) *The Cambridge Examination for Mental Disorders of the Elderly*. Cambridge: Cambridge University Press.

SHIBAYAMA, H., KASAHARA, Y. & KOBAYASHI, H. (1986) Prevalence of dementia in a Japanese elderly population. *Acta Psychiatrica Scandinavica*, **74**, 144–151.

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Mania in the elderly

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A retrospective study of 92 patients admitted with mania, aged over 65 years of age, found that 26% had no prior history of affective illness; 30% had previously only experienced depression, and half of these had at least three episodes of depression before the first manic illness. Patients with a family history of affective disorders had a significantly earlier age of onset of illness. There was evidence of cerebral organic impairment in 24% of the patients, and this group had a significantly later age of onset of illness. Prognosis was good, with only 8% still in hospital at six months. Half of the patients were started on lithium prophylaxis, but this did not significantly alter the number of readmissions. A quarter of those started on lithium developed evidence of lithium toxicity.

Whereas depression in elderly patients is acknowledged to be common, mania has been considered a rare condition (Perris, 1966; Loranger & Levine, 1978). This view is not supported by two studies which have used Department of Health statistics to investigate the age at which patients were admitted to hospital with their first manic illness. Both Spicer *et al* (1973) and Eagles & Whalley (1985) found an increase in the inception rate for mania with advancing age. This was particularly marked after the age of 75 years.

Shulman & Post (1980) studied 67 elderly bipolar patients. Forty-two of these had initially presented with depression and more than half of this latter group had three or more depressions before developing mania, often many years after the first illness.

There is general agreement that for both unipolar and bipolar disorder late-onset patients have a lower incidence of family history of affective illness, although definitions of a late-onset case have varied from 20 to 50 years of age (Hopkinson, 1964; James, 1977; Baron *et al*, 1981; Glassner & Haldipur, 1983).

There has been recent interest in the concept of secondary mania, and Krauthammer & Klermann (1978) comprehensively reviewed the literature concerning mania as a secondary illness. In single case reports mania has been described secondary to L-dopa, procyclidine and steroid medications, to infections such as influenza, Q fever and St Louis Type A encephalitis, and to space-occupying lesions such as meningioma, subarachnoid haemorrhage and metastases, these latter usually occurring in the non-dominant hemisphere (Oppler, 1950; Glaser, 1953; Ryback & Schwab, 1971; Steinberg *et al*, 1972; Schwartz, 1974; Weisart & Hendrie, 1977; Jamieson & Wells, 1979; Cohen & Niska, 1980; Coid & Strang, 1982).

In elderly patients with bipolar disorder, Shulman & Post (1980) found some evidence of cerebral organic disorder in 16 out of 67 patients (24%) with conditions such as cerebrovascular accident (CVA), trauma and Guillain-Barré syndrome. Only three patients had dementia. The authors suggested that organic factors may precipitate mania in some elderly patients.

Lithium treatment has been found to be effective in the elderly (Angst *et al*, 1970; Himmelhoch *et al*, 1980). However, the latter study found that elderly patients with neurological deficit responded poorly and suffered a high incidence of lithium toxicity. Murray *et al* (1983) found that between the fourth and eighth decade there was a 34% reduction in the lithium dosage required to give the same plasma level.

The prognosis for elderly manic patients has only been described in studies which take affective illness as a whole. There appears to have been an improvement in the last few decades. Roth (1955) found that 52% of admissions with affective psychosis were discharged at six months; whereas Blessed & Wilson (1982) described 80% discharged by six months and Christie (1982) reported 91% discharged.

The present study examines various aspects of mania in the elderly such as prior history, prognosis, and lithium treatment. Two-tailed tests are used to compare differences between groups.

The hypothesis that late age of onset is associated with less family history and more organic impairment is examined using one-tailed tests.

Method

A computer search was made of all in-patients aged 65 years and over who were admitted to the Royal Edinburgh and Victoria Hospitals over a ten-year period (1972–81) with a diagnosis of mania. Their case notes were reviewed and patients were included in the study only if they satisfied Feighner's criteria (Feighner *et al*, 1972) for the diagnosis of mania. Further details were elicited from the case notes with regard to the following areas:

(a) index admission (the first admission with mania after the age of 65) and also previous and subsequent episodes of affective illness
(b) lithium treatment and, in particular, evidence of lithium toxicity
(c) family history of affective illness
(d) evidence of cerebral organic impairment; this was only recorded if it fell into one of the following categories:
  (i) disease known to be associated with cerebral pathology, e.g. Parkinson's disease
  (ii) presence of gross cerebral pathology, e.g. CVA occurring during the admission or not more than six months preceding it
  (iii) presence of disorganised cerebral function such as *grand mal* epilepsy or coma, provided this occurred during the admission or in the week preceding it
  (iv) presence of persisting cognitive deficit such as confusion, and short-term memory impairment provided this persisted throughout the admission and did not resolve as the mania responded to treatment.

Results

Index admission data

A total of 92 cases were found, comprising 63 female and 29 male, a ratio of 2.17 : 1. The age range was from 65 to 82, with a mean of 70.3 years. The average length of index admission was 5.4 weeks. Only five patients failed to be discharged from hospital: these all remained as in-patients with chronic relapsing mania until their deaths, which occurred from 2 to 13 years later.

Of those who were discharged, only two had admissions which approached six months in length. Thus, 85 out of 92 patients were discharged by six months.

Previous history of affective illness

Twenty-four of the patients (26%) had no previous history of affective illness. Twelve had previous episodes of mania and 29 had experienced only episodes of depression prior to the index admission.

The mean age of onset of affective illness was 57 years (range 16–82). There was no significant difference relating either to sex or whether the first episode of illness was mania or depression.

In the 29 patients who had experienced only episodes of depression previously, the mean latency period to the first manic illness was 16 years. Fourteen of these patients had experienced three or more episodes of depression prior to their first mania.

Follow-up and readmission data

Eight patients had no follow-up and the remainder had from one month to ten years, with a mean of 3.2 years.

During the follow-up period 47 patients (51%) required readmission, with a total of 117 readmissions between them.

TABLE I
Number of readmissions with affective illness

Number of readmissions (0–10)	*Patients with no previous history (n = 24)*	*Patients with history of affective illness (n = 63)*
0	13	27
1	9	17
2	1	8
3	0	0
4	1	3
5+	0	8

Mann–Whitney U test: $Z = 1.619$ (corrected for ties), $P = 0.1$.

Table I compares the number of readmissions in patients with and without a prior history of affective illness. It can be seen there is no overall significant difference between these groups, although it is noteworthy that those patients with a previous history appear more likely to have a large number of readmissions.

Fifteen patients (16%) had died within two years of discharge.

Lithium treatment

Lithium treatment was commenced in the five chronic in-patients, with no evidence of benefit. Forty-three of the remaining 87 patients were started on lithium prophylaxis. Of these, 19 patients had no readmissions, 14 had one readmission, and the group as a whole had 47 readmissions (mean number per patient, 1.1; mean length of time readmitted, 2.3 months).

Of the 44 patients not started on lithium, 21 had no readmissions, 13 had one readmission, and the group together had 69 readmissions (mean number per patient, 1.6; mean length of time readmitted, 3.0 months).

There were no significant differences in readmissions between the two groups (Mann–Whitney U test, $Z = 0.236$, $P = 0.41$).

One patient developed a goitre while taking lithium, and eleven patients developed lithium toxicity. In nine of the cases, symptoms of lithium toxicity were present and lithium levels ranging from 1.4 mmol/l to 2.6 mmol/l were documented. In the other two cases symptoms of tremor, vomiting and ataxia were present. These resolved on stopping lithium, but lithium levels were not recorded.

Five lithium-toxic patients required admission with symptoms of acute confusional state.

Family history

Eighty-three patients had sufficient details in their case notes for a decision to be made as to whether a family history of affective illness was present or absent, and 22 patients had a positive family history. Seven patients had two first-degree relatives affected and the remainder only had one.

The age of onset of illness was uncertain in one patient. In the remaining 82 patients, those with a family history

TABLE II
Age at onset of affective illness and its relationship to family history

	Patients with no family history	*Patients with a family history*
Patients aged <30 at onset	1	2
Patients aged 30–39 at onset	4	3
Patients aged 40–49 at onset	7	3
Patients aged 50–59 at onset	14	7
Patients aged 60–69 at onset	16	6
Patients aged 70+ at onset	18	1
Age at onset		
Mean	60.4	53.1
Median	63	55

$t=2.10$, d.f. $=80$, $P<0.025$.

had a significantly earlier age of onset. Table II gives further details.

Cerebral organic impairment

Persisting clinical evidence of cerebral organic impairment was found in 22 of the 92 patients. Fourteen patients had memory impairment, usually a specific short-term memory loss, and six of this group also had persisting disorientation and confusion. CT scans were performed on three patients and in each case they confirmed generalised cortical atrophy. During the follow-up period only three of the fourteen went on to develop dementia of a moderate to severe degree.

The remaining eight patients with cerebral organic impairment had a variety of more specific conditions. One of these had Parkinson's disease and another an intention tremor and facial dyskinesia. Two patients had a CVA, one of these, on the right side, occurring four months prior to the index admission, and the other, affecting the left internal capsule, developing in the second week of the admission. Three patients who were not previously epileptic had *grand mal* seizures: in one case this occurred on the day before admission and in the other two during the admission; one of the latter cases also had slurred speech and facial dyskinesia and the other had CT-scan evidence of dilated third and lateral ventricles. The eighth patient became disorientated, confused and semi-comatose during the index admission; this resolved with no definite diagnosis being made.

Three of these eight cases had no previous history of affective illness and would satisfy Krauthammer & Klermann's (1978) criteria for secondary mania.

TABLE III
Age at onset of affective illness and its relationship to cerebral organic impairment

	Patients with no cerebral impairment (n=70)	*Patients with cerebral impairment (n=21)*
Patients aged <30 at onset	3	2
Patients aged 30–39 at onset	7	0
Patients aged 40–49 at onset	13	1
Patients aged 50–59 at onset	19	4
Patients aged 60–69 at onset	15	8
Patients aged 70+ at onset	13	6
Age at onset		
Mean	56.0	61.0
Median	55.5	67

Mann–Whitney U test: $Z=1.946$, $P=0.026$.

The age of onset of affective illness in those patients with cerebral organic impairment was found to be significantly later than in the remaining patients. Details are given in Table III. Only two patients with cerebral organic impairment also had a family history of affective illness.

The patients with cerebral organic impairment did not differ significantly from the remaining patients on any of the following parameters: clinical features of mania, number of readmissions, response to lithium, or percentage dying within a two-year follow-up.

Discussion

The mean age of onset of affective illness was 58 years: this contrasts strikingly with the results of other workers (Carlson *et al*, 1977; Baron *et al*, 1981), who have found a mean age of onset of less than 30 years.

Shulman & Post (1980), who also studied an elderly cohort, found a later age of onset of 49 years. It may be, as Winokur (1975) has suggested, that a proportion of affective illness 'burns out' with age, so is not included in an elderly sample.

One-quarter of the patients in this study first became ill after the age of 65, and both Spicer *et al* (1973) and Eagles & Whalley (1985) found a raised inception rate for mania with increasing age, particularly after 75 years. As the elderly population increases in the next decade it seems likely that there will be more manic patients requiring resources from psychogeriatric services.

Fourteen out of 29 patients (48%) with a previous history solely of depression had at least three episodes before the index admission with mania. Exactly the same percentage was found by Shulman & Post (1980), although they found a mean latency period of 10 years to the first manic episode, compared with 16 years in the present study. These findings contrast with Perris's (1966) figure of 16% for patients who 'convert' to bipolar after three episodes of depression. One reason for this difference is that patients who remained unipolar were not included in the present study. It is striking, however, that some of the present cohort of patients would have been wrongly classified for a long period of time.

Lithium was used in the initial treatment of mania in one-fifth of the cases and for prophylaxis in a half. This latter group did not differ significantly in the number or length of readmissions from the patients not started on lithium, although since the patients were not randomly allocated for lithium treatment no firm conclusions about its efficacy can be drawn. The majority of studies showing the value of lithium prophylaxis have had a lower mean age of patient (Angst *et al*, 1970; Coppen *et al*, 1971), but Shulman & Post (1980) gained a "strong impression of the usefulness of lithium in bipolar patients aged 60 years and over". Also Himmelhoch *et al* (1980) found that the majority of 81 elderly bipolar patients responded well to lithium, the exceptions being 17 patients with cerebral organic impairment, who were not only poor responders but more likely to develop lithium toxicity.

In the present study, cerebral organic impairment had no effect on either response to lithium or toxicity. The type of impairment appears to be different, however, with Himmelhoch *et al* identifying 12 patients with extrapyramidal symptoms who were all included in the group of 19 patients who developed chronic mania. This contrasts with two patients with extrapyramidal symptoms and only five who developed chronic mania in this study.

A quarter of the 45 patients started on lithium developed lithium toxicity with lithium levels of 1.4–2.6 mmol/l, and five of these required admission with an acute confusional state. This is a considerably greater percentage than the 13% with lithium toxicity described by Roose *et al* (1979) in 31 patients over the age of 60.

Murray *et al* (1983) found a 34% reduction with advanced age in the lithium dosage required to produce a therapeutic level. The present study underlines the need for careful monitoring of lithium levels in this age group, even in those without antecedent cerebral damage.

It is now well documented that early onset of affective illness is associated with an increased genetic component, as demonstrated by family history (Hopkinson & Ley, 1969; Baron *et al*, 1981) and Smeraldi *et al* (1983) have suggested that age of onset is an index of penetrance variability. Different workers have used different ages between 20 and 50 years to divide early- and late-onset cases, however. In the present study a progressive decrease in family history with advancing age of onset was noted, with the biggest decrease after 70 years.

With increasing evidence that first episodes of mania can occur in advanced old age it may be necessary to reconsider the age before which a patient should be thought of as an early-onset case. The present findings support the suggestion made by Shulman & Post (1980) that 50 years rather than 20 or 30 might be more appropriate in this respect.

Another finding in common with Shulman & Post is that 24% of the patients had evidence of cerebral organic impairment. There was also an excess of male patients (31%) compared with female (22%), but in contrast with the results of Shulman & Post this did not reach statistical difference.

Although 14 patients had generalised cortical atrophy, only three of the 92 patients went on to develop well-documented dementia over the follow-up period. It now seems clear that in elderly patients with either unipolar or bipolar affective disorder there is a normal incidence of dementia (i.e. they develop dementia no more than one would expect by chance) (Kay *et al*, 1955; Shulman & Post, 1980; Baldwin & Jolley, 1986).

Eight patients had more specific localised evidence of cerebral dysfunction, and three of these had no previous history of affective disorder and would satisfy Krauthammer & Klermann's (1978) criteria for secondary mania.

The patients with organic impairment had a significantly later age of onset of illness and only two of them had a family history of illness. This supports the hypothesis that there may be two overlapping populations who suffer from mania: those with a genetic component as evidenced by family history, who develop the illness early in life; and those with no (or a smaller) genetic component, who are precipitated into illness by cerebral organic impairment in later life.

Tsuang *et al* (1985) proposed a common-aetiology model for affective illness with a lower threshold for depression and a higher threshold for mania. This would be consistent with the present result that the mean latency from first depression to first mania was 16 years. Also, only five of the 22 patients with cerebral organic impairment had a prior history of mania, eight having no previous history and nine having experienced only episodes of depression. In some of these cases it may be that organic factors occurring in old age caused them to exceed the higher threshold and develop a manic illness for the first time.

The link between organicity and onset of illness is less clear-cut in this group of patients than in the three cases of secondary mania, but it is a much larger group and it seems likely that in elderly manic patients the role of organic impairment as part of a multifactorial aetiology will be increasingly recognised.

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References

Angst, J., Weis, P., Grof, P., *et al* (1970) Lithium prophylaxis in recurrent affective disorders. *Acta Psychiatrica Scandinavica*, **46**, 604–613.

Baldwin, R. C. & Jolley, D. J. (1986) The prognosis of depression in old age. *British Journal of Psychiatry*, **149**, 574–583.

Baron, M., Mendelwicz, J. & Klotz, J. (1981) Age of onset and genetic transmission in affective disorders. *Acta Psychiatrica Scandinavica*, **64**, 373–380.

Blessed, G. & Wilson, I. D. (1982) The contemporary natural history of mental disorder in old age. *British Journal of Psychiatry*, **141**, 59–67.

Carlson, G. A., Davenport, Y. B. & Jamison, K. (1977) A comparison of outcome in adolescent- and late-onset bipolar manic–depressive illness. *American Journal of Psychiatry*, **134**, 919–921.

Christie, A. B. (1982) Changing patterns in mental illness in the elderly. *British Journal of Psychiatry*, **140**, 154–159.

Cohen, M. R. & Niska, R. W. (1980) Localised right cerebral hemisphere dysfunction and recurrent mania. *American Journal of Psychiatry*, **137**, 847–848.

Coid, J. & Strang, J. (1982) Mania secondary to procyclidine (Kemadrin) abuse. *British Journal of Psychiatry*, **141**, 81–83.

Coppen, A., Noguera, R. & Bailey, J. (1971) Prophylactic lithium in affective disorders: controlled trial. *Lancet*, *ii*, 275–279.

Eagles, J. M. & Whalley, L. J. (1985) Ageing and affective disorders: the age at first onset of affective disorders in Scotland, 1969–1978. *British Journal of Psychiatry*, **147**, 180–187.

Feighner, J., Robins, E., Guze, S., *et al* (1972) Diagnostic criteria for use in psychiatric research. *Archives of General Psychiatry*, **26**, 57–63.

Glaser, G. H. (1953) Psychotic reactions induced by corticotrophin (ACTH) and cortisone. *Psychosomatic Medicine*, **15**, 280–291.

Glassner, G. & Haldipur, C. V. (1983) Life events and early and late onset of bipolar disorder. *American Journal of Psychiatry*, **140**, 215–217.

Himmelhoch, J. M., Neil, J. F., May, S. J., *et al* (1980) Age, dementia, dyskinesis, and lithium response. *American Journal of Psychiatry*, **137**, 941–945.

Hopkinson, G. (1964) A genetic study of affective illness in patients over fifty. *British Journal of Psychiatry*, **110**, 244–254.

—— & Ley, P. (1969) Genetic study of affective disorders. *British Journal of Psychiatry*, **115**, 917–922.

James, H. M. (1977) Early and late onset bipolar affective disorder: a genetic study. *Archives of General Psychiatry*, **34**, 715–717.

Jamieson, R. C. & Wells, C. E. (1979) Manic psychosis in a patient with multiple metastatic brain tumours. *Journal of Clinical Psychiatry*, **40**, 280–283.

Kay, D. W. K., Roth, M. & Hopkins, B. (1955) Affective disorders arising in the senium–1. Their association with organic cerebral degeneration. *Journal of Mental Science*, **101**, 302–315.

Krauthammer, C. & Klermann, G. L. (1978) Secondary mania: manic syndromes associated with antecedent physical illness or drugs. *Archives of General Psychiatry*, **35**, 1333–1338.

Loranger, A. W. & Levine, P. M. (1978) Age at onset of bipolar affective illness. *Archives of General Psychiatry*, **35**, 1345–1348.

Murray, N., Hopwood, S., Balfour, D. J. K., *et al* (1983) The influence of age on lithium efficiency and side-effects in outpatients. *Psychological Medicine*, **13**, 53–60.

Oppler, W. (1950) Manic psychosis in a case of parasagittal meningioma. *Archives of Neurology and Psychiatry*, **64**, 417–430.

Perris, C. (1966) A study of bipolar (manic depressive) and unipolar recurrent depressive psychosis. *Acta Psychiatrica Scandinavica*, **42**, (suppl. 194), 1.

Roose, S. P., Bone, S., Haidorfer, C., *et al* (1979) Lithium treatment in older patients. *American Journal of Psychiatry*, **136**, 834–844.

Roth, M. (1955) The natural history of mental disorder in old age. *Journal of Mental Science*, **101**, 281–301.

Ryback, R. S. & Schwab, R. S. (1971) Manic response to levodopa. *New England Journal of Medicine*, **285**, 788–789.

Schwartz, R. B. (1974) Manic psychosis in connection with Q fever. *British Journal of Psychiatry*, **124**, 140–143.

Shulman, K. & Post, F. (1980) Bipolar affective disorder in old age. *British Journal of Psychiatry*, **136**, 26–32.

Smeraldi, E., Gasperini, M., Macciardi, F., *et al* (1983) Factors affecting the distribution of age at onset in patients with affective disorders. *Journal of Psychiatric Research*, **17**, 309–317.

Spicer, C. C., Hare, E. H. & Slater, E. (1973) Neurotic and psychotic forms of depressive illness: evidence from age-incidence in a national sample. *British Journal of Psychiatry*, **123**, 535–541.

Steinberg, D., Hirsch, S. R., Marston, S. D., *et al* (1972) Influenza infection causing manic psychosis. *British Journal of Psychiatry*, **120**, 531–535.

Tsuang, M. T., Faraone, S. V. & Fleming, J. A. (1985) Familial transmission of major affective disorders: is there evidence supporting the distinction between unipolar and bipolar disorders? *British Journal of Psychiatry*, **146**, 268–271.

Weisart, K. N. & Hendrie, H. C. (1977) Secondary mania: a case report. *American Journal of Psychiatry*, **134**, 140–143.

Winokur, G. (1975) The Iowa 500: heterogeneity and course in manic depressive illness (bipolar). *Comprehensive Psychiatry*, **16**, 125–131.

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Schizophrenia and the Perception of Emotions
How Accurately do Schizophrenics Judge the Emotional States of Others?

P. CRAMER, M. WEEGMANN and M. O'NEIL

Audiovisual tapes of emotional situations were shown to 34 schizophrenics and 15 controls who were asked to rate the emotional content of the scenes using an adjective check-list. The schizophrenic patients failed to detect the dominant character of the scenes, and perceived the opposite emotions to those perceived by the controls. Such deviant responses were not related to paranoid symptoms, flattened affect, formal thought disorder, general level of morbidity, or duration of in-patient stay.

Studies examining the judgement of the emotional states of others by schizophrenics using photographs (Izard, 1959; Dougherty *et al*, 1974; Muzekari & Bates, 1977; Walker *et al*, 1980; Cutting, 1981) and audio material (Turner, 1964; Jonsson & Sjostedt, 1973) have uniformly found a marked discrepancy between the assessments of schizophrenic patients and normal controls. The application of personal construct theory (Kelly, 1955) to schizophrenic patients (Bannister, 1960, 1962) showed a greater disruption in psychological construing than in object construing (McPherson *et al*, 1970; Bannister & Salmon, 1966; Williams & Quirke, 1972; McPherson *et al*, 1975; Bodlakovȧ *et al* 1974). However, there is little agreement as to whether the phenomenon is a product of the impoverished social environment of the long-stay patient (Williams & Quirke, 1972; Walker *et al*, 1980), a selective inattention to psychological factors (Pilowsky & Basset, 1980), the acute phase of a schizophrenic illness (Cutting, 1981), flattened affect (McPherson *et al*, 1970, 1975; Bodlakova *et al*, 1974), or thought disorder (Bannister & Salmon, 1966).

Much of the confusion can be attributed to the fact that no single study has examined all of the potentially relevant factors listed above at one time. In addition, there has been a persistent failure to employ clear-cut diagnostic criteria or to consider the general level of morbidity. This has produced contradictory results in the literature such that it is possible to find reports suggesting that schizophrenics with paranoid symptoms are both superior (La Russo, 1978) and inferior (Izard, 1959) to controls in the judgement of facial expressions.

This study tested the hypothesis that schizophrenic patients meeting clear-cut diagnostic criteria misjudge the emotional states of others. We used the more realistic material of videotaped scenes of social interactions, a method not used in this area before. Furthermore we hypothesised that the problem is related directly to the illness itself, rather than being a product of institutionalisation, a phenomenon secondary to particular symptoms such as blunted affect, paranoid thinking, or thought disorder, or related to the general level of morbidity.

Method

Subjects

The subject population consisted of 15 controls and 34 schizophrenic in-patients (23 men, average age 37, and 11 women, average age 38). Fifteen patients were classified as 'short-stay' (less than one year). All the patients met Research Diagnostic Criteria for schizophrenia (Spitzer *et al*, 1975).

The subjects were also screened using the Schonnel Reading Test, a guide to pre-morbid IQ (Nelson & McKenna, 1975). The general level of morbidity, paranoid symptoms, and formal thought disorder was rated using the Brief Psychiatric Rating Scale (BPRS; Overall & Gorham, 1962): 13 patients had paranoid symptoms, and 10 patients had thought disorder. The schizophrenic population was further divided by the presence or absence of affective flattening, using a scale taken from Wing & Brown (1970). The opinion of nursing staff was sought in evaluating the scoring on this scale. For our purposes, to rate flatness as being present a patient had to score four or five on the six-point scale, that is, 'mostly flat', or 'completely flat': there were six blunted patients in the short-stay group, and four in the long-stay group. One patient could not be assessed on his affective status owing to non-compliance.

The 15 controls were matched for age and sex, and were drawn from the hospital staff from a range of disciplines.

Video scenes

Each patient was shown a video containing five scenes (A–E) each involving two actors, one facing the camera, the other with his back to it. Scene A showed an anxious woman planning to cook a meal for the man in the scene, who was encouraging her; scene B, an angry father being critical of his daughter; scene C, a mother showing disapproval of her son staying in bed all day; scene D, a mother complaining of being ashamed of her son's rudeness to others; scene E, a woman encouraging an uncertain man about his painting.

Procedure

The scenes were shown in random order. The video was originally only intended for use in training raters of high expressed emotion. It was scripted to show the following range of interactions, which we gave as a check-list to the subjects: concern, interfering, happy, ashamed, encouraging, angry, relaxed, worried, sad, scornful, interested, disapproving, and surprised. The subjects were asked to select the four adjectives which most applied to the emotional state of the principal actor for each scene. They were also asked to rank them in order of importance.

Three scores were derived: a global score, a deviancy score, and a sensitivity score. The adjectives had already been divided by the researchers into those which had a critical and/or unpleasant connotation and those which did not. The rankings were added, taking the connotations into account by giving a negative or positive sign to the adjective's ranking depending on whether the adjective was viewed as critical/unpleasant or non-critical/pleasant, respectively. This generated a global score varying between +10 and −10.

The reliability of the global scoring system was examined by taking the two components of the system separately, that is the valence of the adjectives and the summation of the rankings. A second control group of ten normal subjects produced a level of 97% agreement on deciding which adjectives had a positive or negative connotation.

Inter-rater reliability was examined in two steps. Differences between scores were dependent on the valence of the adjectives chosen. The rankings can make a difference to a particular rater's score only if a mixture of positive and negative adjectives are included. Our impression was that the scenes were unambiguously positive or negative, and hence the adjectives used by the raters for each scene should be either all positive or all negative. In fact at least 98% of the responses on the positive films were positive, and 90% of the ratings on the negative films were negative. Thus detailed examination of the precise rankings was unnecessary.

A deviant response was defined as being one where the dominant adjective given by the subject for a particular scene had a connotation contrary to the global opinion of the controls for that scene. The 'global opinion' was equated with the sign of the mean score of the controls for the scene. In other words a deviant response involved a first choice of a critical adjective in a non-critical scene as judged by the controls, or vice versa. This assumed that the scenes could be unambiguously partitioned into critical and non-critical ones. This was borne out by the means (and standard deviations) of the controls' ratings: 9.1 (2.1), −9.08 (1.3), −6.0 (3.0), −9.06 (1.5), and 9.8 (0.04) for the scenes A, B, C, D, and E respectively.

The sensitivity score was assessed using the frequency with which schizophrenics rated as dominant the dominant emotion judged by the controls. This was to determine whether there was selective inattention to some emotions, as suggested by Dougherty *et al* (1974).

We found substantial inter-rater reliability on the first and second rankings; for example, 70% for scene A, and 60% for scene B, the former being a positive film, the latter a negative one. Differences between raters tended to take the form of interchanging the order of the first and second choice of adjectives.

Statistical analysis

As the scores were actually rankings or frequency of responses, a non-parametric statistical analysis was carried out, primarily using the χ^2 test to compare the scores between the different groups and subgroups. Only the deviancy score was used in examining differences within the schizophrenic group, as the numbers of such responses were large enough to make such comparisons meaningful. The global scores were compared by calculating a mean global score for the total group, that is both patients and controls, and then comparing the numbers scoring above and below this mean for the two classes using the χ^2 test.

Results

The total population means for scenes A, B, C, D, and E were 7.6, −7.2, −5.0, −6.0, and 7.9 respectively. The distribution about these means for each scene are shown in Table I. The differences are significant on scenes D ($\chi^2 = 12.58$, $P < 0.001$) and E ($\chi^2 = 7.58$, $P < 0.01$), and approach significance on scene B.

Sensitivity

The dominant adjectives for the scenes, as judged by the controls, were A encouraging, B angry, C disappointed, D ashamed, and E encouraging. Table II shows the numbers applying each of these terms in each scene. These differences are significant for scenes A ($\chi^2 = 4.61$, $P < 0.05$), C ($\chi^2 = 4.12$, $P < 0.05$), and D ($\chi^2 = 11.54$, $P < 0.001$). The two scenes where the differences were not significant were also those scenes which the controls judged the most negative (scene B) and the most positive (scene E) on global scoring.

TABLE I

The global scores' distribution about the population mean for schizophrenics and controls by video scene

Video scene	*Schizophrenics (n = 34)*		*Controls (n = 15)*	
	Less than mean	*Greater than mean*	*Less than mean*	*Greater than mean*
A	12	22	2	13
B	18	16	13	2
C	16	18	10	5
D	14	20	15	0
E	15	19	0	15

TABLE II
Sensitivity by video scene

Video scene	*Dominant adjective*	*Number of responses* Controls (n=15)	Schizophrenics (n=34)
A	Encouraging	9	8
B	Angry	11	17
C	Disappointed	5	2
D	Ashamed	7	1
E	Encouraging	9	9

Deviancy

The controls produced three deviant responses out of 75 first responses, and the schizophrenics produced 44 from 170, a significant difference ($\chi^2 = 14.72$, $P < 0.001$). Only on scene D, where the schizophrenics produced 17 deviant responses to nil by the controls, was the difference statistically significant ($\chi^2 = 7.50$, $P < 0.01$).

The median score on the BPRS was 10. There were seven low scorers ($\leqslant 5$) and six high scorers ($\geqslant 14$). There was no significant difference in deviancy scores between these two groups. There was also no significant association between high and low scores on the BPRS and the duration of in-patient stay. There was no statistically significant difference between patients who did and did not have paranoid symptoms, formal thought disorder, or flattened affect. There was no association between deviancy and duration of in-patient stay. There was no association between any of the scores and age or sex.

Discussion

On all three measures, global responding, deviant responding, and sensitivity, the schizophrenic group as a whole judged the scenes differently to the controls. The patients erred in two ways: inaccurately judging the emotional content of the scene, and reading an emotional content into the scenes which conflicted with the general view of the scenes taken by the controls. It is of note that the two scenes which the controls viewed as most strongly positive (E) and negative (B) were the scenes in which the sensitivity score found no difference between the schizophrenics and controls. It would seem that even the smallest degree of ambiguity results in the schizophrenic population producing errors. The results support our hypothesis that the effect is not merely a by-product of institutionalisation, but is related to the diagnosis rather than to particular symptoms within a schizophrenic population or to the general level of morbidity.

The original design included a depressive group to act as psychiatric controls, but, unfortunately, we collected too few patients to carry out any meaningful statistical analysis. This omission leaves open the question of how specific our findings are to schizophrenia. As in most studies in this area, we were not able to examine the relationship between medication and the patients' responses. The patients were not part of a trial, and hence their drug regimes varied widely, not just in neuroleptic dosage, but also in the type of drug being administered. We did not feel it valid to compare such heterogeneous drug regimes. However, one would expect that there would be a positive correlation between the level of medication and the level of morbidity, and so an association between the latter and the ratings. No such association was found.

There are a number of other factors which must be considered. Firstly, the method relies upon introspective reports to carry out a classificatory task. Such a task could be disrupted by schizophrenic idiosyncrasies in the use of language. However, such idiosyncrasies would be most manifest in patients who had formal thought disorder, and there was no association between formal thought disorder and deviancy scoring. Furthermore, there was no association between the general level of morbidity and the patients' scores. This would argue against the problem being essentially a linguistic one.

A more difficult criticism to rebut is that the scoring of the schizophrenic patients is paradoxical, in that they are so vulnerable at some level to the emotional states of others that they are using a mental mechanism (e.g. denial), so that the scores do not reflect what the patient is actually experiencing. This study cannot refute such an argument. However, if one accepts that relapse rates in psychiatric populations in the face of high expressed emotion (EE) are an index of vulnerability to the emotional states of others, then one could argue, following Vaughn & Leff (1976), that schizophrenics are not the most vulnerable patient group.

The initial aim was to derive a single score to measure the accuracy in judging emotional communication. However, this created a problem of interpretation, and hence resulted in the development of sensitivity and deviancy scores to see whether the problem was one of aberrant or insensitive responding. In retrospect, it might have been simpler to use bipolar scales or a separate present/absent dichotomy for each adjective plus an independent rating scale for each adjective rather than tying all the adjectives together with a ranking system.

It might be argued that this study has little relevance to the work on high EE, as judging scenes with actors is rather different from judging the emotional communication of a relative. However, although there is evidence that the disruption of psychological construing in schizophrenic patients is less when the material presented involves names of relatives, there is still a significant problem (Williams, 1971). On the other hand, the psychophysiological studies with schizophrenic patients with high- and low-EE relatives could be interpreted as evidence for the capacity of schizophrenics to interpret accurately the emotional states of relatives (Tarrier *et al*, 1979, 1988; Sturgeon *et al*, 1981, 1984). However, there is no consensus in these studies as to whether the entry of a high-EE relation during testing produces a specific impact on arousal. Furthermore, the uttering of a critical comment did not produce a significant change in arousal (Sturgeon *et al*, 1981). Additionally, there was substantial variation in arousal when EE was controlled for (Sturgeon *et al*, 1984).

If our results are combined with those of Tarrier *et al* (1988), in particular the failure of different dimensions of EE to produce different psychophysiological responses and the disjunction between the patient's reports of his own emotional state and measures of arousal, then this would suggest a global impairment of the capacity to judge emotional states. Such a deficit would tend to magnify subjectively the unpredictability correlated with EE (McCarthy *et al*, 1986) and to produce inappropriate social responses to EE by the patient, leading to a vicious cycle of spiralling EE in the face of apparent indifference together with a failure of the patient to reduce his level of face-to-face contact.

The study raises issues for further research: firstly, to examine whether the problems in the judgement of emotional states of others are specific to schizophrenia as opposed to other psychiatric conditions, and, secondly, to examine the relationship of interactions within the families of schizophrenic patients to their failure to judge emotional states accurately.

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References

BANNISTER, D. (1960) Conceptual structure in thought disordered schizophrenics. *Journal of Mental Science*, **106**, 1230–1249.

—— (1962) The nature and measurement of schizophrenic thought disorder. *Journal of Mental Science*, **108**, 825–842.

—— & SALMON, E. (1966) Schizophrenic thought disorder, specified or diffuse? *British Journal of Medical Psychology*, **39**, 215–219.

BODLAKOVA, V., HEMSLEY, D. & MUMFORD, D. (1974) Psychological variables and the flattening of affect. *British Journal of Medical Psychology*, **47**, 227–234.

CUTTING, J. (1981) Judgement of emotional expressions in schizophrenics. *British Journal of Psychiatry*, **139**, 1–6.

DOUGHERTY, F., BARTLETT, E. & IZARD, C. (1974) Responses of schizophrenics to expressions of the fundamental emotions. *Journal of Clinical Psychology*, **30**, 243–246.

IZARD, C. (1959) Paranoid schizophrenic and normal subjects' perception of photographs of human faces. *Journal of Consulting Psychology*, **23**, 119–124.

JONSSON, C. O. & SJOSTEDT, A. (1973) Aural perception in schizophrenia, a second study of the intonation test. *Acta Psychiatrica Scandinavica*, **49**, 558–600.

KELLY, G. (1955) *Psychology of Personal Constructs*. New York: Norton.

LA RUSSO, L. (1978) Sensitivity of paranoid patients to non-verbal cues. *Journal of Abnormal Psychology*, **87**, 463–471.

MACCARTHY, B., HEMSLEY, D., SCHRANK-FERNANDEZ, C., *et al* (1986) Unpredictability as a correlate of expressed emotion in the relatives of schizophrenics. *British Journal of Psychiatry*, **148**, 727–731.

MCPHERSON, F. M., BARDEN, V., HAY, J., *et al* (1970) Flattening of affect and personal constructs. *British Journal of Psychiatry*, **116**, 39–43.

——, ARMSTRONG, J. & HEATHER, B. B. (1975) Psychological construing; "difficulty" and thought disorder. *British Journal of Medical Psychology*, **48**, 303–315.

MUZEKARI, L. & BATES, M. (1977) Judgement of emotion among chronic schizophrenics. *Journal of Clinical Psychology*, **33**, 662–666.

NELSON, H. & MACKENNA, P. (1975) The use of current reading ability in the assessment of dementia. *British Journal of Social and Clinical Psychology*, **14**, 259–267.

OVERALL, J. & GORHAM, D. (1962) The Brief Psychiatric Rating Scale. *Psychological Reports*, **10**, 799–812.

PILOWSKY, I. & BASSETT, D. (1980) Schizophrenia and response to facial emotions. *Comprehensive Psychiatry*, **1**, 236–244.

SPITZER, R., ENDICOTT, J. & ROBBINS, P. (1975) *Research Diagnostic Criteria*. Instrument number 58. New York: New York State Psychiatric Institute.

STURGEON D., KUIPERS, L., BERKOWITZ, R., *et al* (1981) Psychophysiological responses of schizophrenic patients to high and low expressed emotion relatives. *British Journal of Psychiatry*, **138**, 40–50.

——, TURPIN, G., BERKOWITZ, R., *et al* (1984) Psychophysiological responses of schizophrenic patients to high and low expressed emotion relatives: a follow-up study. *British Journal of Psychiatry*, **145**, 62–69.

TARRIER, N., VAUGHN, C. E., LADER, M. H., *et al* (1979) Bodily reactions to people and events in schizophrenia. *Archives of General Psychiatry*, **36**, 311–315.

——, BARROWCLOUGH, C., PORCEDDU, K., *et al* (1988) The assessment of physiological reactivity to the expressed emotion of the relatives of schizophrenic patients. *British Journal of Psychiatry*, **152**, 618–624.

TURNER, J. (1964) Schizophrenics as judges of vocal expressions of emotional meaning. In *The Communication of Emotional Meaning* (ed. J. Davy). New York: McGraw Hill.

VAUGHN, C. E. & LEFF, J. P. (1976) The influence of family and social factors on the course of psychiatric illness. *British Journal of Psychiatry*, **129**, 125–137.

WALKER, E., MARWIT, S. & EMORY, E. (1980) A cross sectional study of emotional recognition in schizophrenics. *Journal of Abnormal Psychology*, **89**, 428–439.

WILLIAMS, E. (1971) The effect of varying elements in the Bannister Fransella grid test of thought disorder. *British Journal of Psychiatry*, **119**, 207–212.

WILLIAMS, J. & QUIRKE, E. (1972) Psychological construing in schizophrenics. *British Journal of Medical Psychology*, **45**, 79–84.

WING, J. & BROWN, G. (1970) *Institutionalisation and Schizophrenia*. Cambridge: Cambridge University Press.

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The Contribution of Problem Drinking to the Level of Psychiatric Morbidity in the General Hospital

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Of 331 patients admitted to a general hospital to whom the CAGE questionnaire was administered, those who scored 2 or more for alcoholism scored higher on a number of measures of psychiatric morbidity than those with a CAGE score of 0. Those patients who scored 1 showed less psychiatric morbidity than those who scored 0. Among the male patients who scored at least one question positively, those who had abstained from alcohol for at least a year showed higher levels of psychiatric morbidity than those still drinking.

Many surveys have been made of psychiatric morbidity in the wards of general hospitals (Mayou & Hawton, 1986), and many surveys have also been carried out on the prevalence of alcoholism or alcohol-related disabilities in the same setting (Jarman & Kellett, 1979; McIntosh, 1982). However, the relationship between the level of psychiatric morbidity in general-hospital wards and the rate of problem drinking does not appear to have been investigated.

This paper looks at the psychological health of patients in two medical wards and one surgical ward in a general hospital, and compares the psychological health of those who scored positively on the CAGE questionnaire for alcoholism (Ewing, 1984) with the psychological health of the other patients in the same wards. It is hoped thereby to assess the contribution of problem drinking to levels of psychiatric morbidity in the general hospital.

Method

All consecutive admissions to a general medical, a general surgical and a neurological ward of the Regional Hospital, Cork, a general hospital with an in-patient psychiatric unit, were surveyed for four weeks each sequentially. Patients who were considered too ill or who failed to give consent were excluded. These wards were chosen to give a cross-section of the general-hospital population.

Each patient was given the CAGE questionnaire (Ewing, 1984) by interview, usually on the day of admission, and was asked to complete overnight the General Health Questionnaire (GHQ–28; Goldberg, 1972), the short form of the Beck Depression Inventory (BDI; Beck & Beck, 1972), and the anxiety scale of the Hospital Anxiety and Depression Scale (HAD; Zigmond & Snaith, 1983).

The CAGE questionnaire is as follows.

(a) Have you ever felt you should cut down on your drinking?
(b) Have people ever annoyed you by criticising your drinking?
(c) Have you ever felt bad or guilty about your drinking?
(d) Have you ever had a drink first thing in the morning to steady your nerves or to get rid of a hang-over (eye-opener)?

The cut-off point for alcoholism on the CAGE is between 2 and 3.

The following definitions are used for the purposes of this study. A 'problem drinker' is one who scores positively on the CAGE questionnaire, whether above or below the cut-off point. An 'alcoholic' is a patient who scores above the cut-off point on the CAGE questionnaire. An 'abstainer' is a patient who has not drunk any alcohol for at least one year. A 'non-drinker' is a patient who has never drunk alcohol.

Results

Of the 407 patients consecutively admitted to the three wards over the 12 weeks, 331 (81%) were administered the CAGE questionnaire. There were 56 males and 11 females who answered at least one question positively (Table I). The GHQ, BDI and HAD were completed successfully by 146 of the 179 males answering the CAGE questionnaire (81%), and 120 of the 152 females (78%) (Tables II and III).

Twenty-four (17%) of the surgical patients, 22 (21%) of the medical patients and 30 (19%) of the neurology patients did not enter the study (see above). Of those patients who completed the CAGE questionnaire, 26 (23%) of the surgery patients, 16 (19%) of the medical patients, and 25 (19%) of the neurology patients failed to complete the GHQ. Those patients who did not complete the

TABLE I
Sex and scores on CAGE questionnaire of 331 patients

CAGE score	*Number of males*	*Number of females*	*Total number of patients*
0	123	141	264
1	25	6	31
2	18	2	20
3	7	3	10
4	6	0	6
Total	179	152	331

TABLE II

CAGE score and mean and standard deviation of GHQ, BDI, and HAD scores in males

			Psychological test score			
Psychological test	*CAGE score*	*Number of males*	*Mean*	*s.d.*	t*	P
GHQ	0	97	4.6	5.3	–	–
	1	22	2.6	2.4	2.7	0.01–0.001
	2	13	7.8	7.4	1.5	0.5–0.1
	3	7	5.9	6.9	0.5	>0.5
	4	6	15.7	7.2	3.7	<0.001
BDI	0	99	3.6	4.5	–	–
	1	22	2.5	3.1	1.4	0.5–0.1
	2	13	6.9	5.4	2.1	0.05–0.02
	3	7	3.1	3.9	0.3	>0.5
	4	6	14.2	10.8	2.4	0.02–0.01
HAD	0	98	4.2	3.7	–	–
	1	22	3.4	2.3	1.3	0.5–0.1
	2	13	8.9	3.5	4.5	<0.001
	3	7	6.7	4.4	1.5	0.5–0.1
	4	6	10.5	5.7	2.7	0.01–0.001

* *t* test: comparison with CAGE 0 group.

TABLE III

CAGE score and mean and standard deviation of GHQ, BDI, and HAD scores in females

			Psychological test score			
Psychological test	*CAGE score*	*Number of females*	*Mean*	*s.d.*	t*	P
GHQ	0	110	5.4	5.8	–	–
	1–4	9	9.7	7.0	1.8	0.1–0.05
BDI	0	111	3.6	4.6	–	–
	1–4	9	7.1	7.7	1.3	0.5–0.1
HAD	0	111	5.7	4.5	–	–
	1–4	9	7.8	4.1	1.5	0.5–0.1

* *t* test: comparison with CAGE 0 group.

psychological questionnaires were usually considered unsuitable to do so even by interview, because of lack of concentration, discomfort, deafness, unwillingness, the priority of medical tests and treatment, and loss to follow-up through transfer to other wards. A small number of test papers were lost, and in three cases relatives objected to the questionnaires, despite the consent of the patients concerned and the provision of a typed sheet giving details of the study. Strenuous efforts were made to explain the study to patients, to trace missing test papers, and to contact relatives where appropriate.

Each score group of males (CAGE 1, 2, 3, 4) and the total positive small group of females (CAGE 1–4) was compared with the CAGE 0 scorers of the same sex, who thus acted as control groups.

The higher the CAGE score, the greater was the psychiatric morbidity, as measured by the GHQ, BDI, and HAD, in both males and females, except for those males who scored 1 on the CAGE. These males had lower levels of psychiatric morbidity than the control group, significantly so on the GHQ.

The seven males with a CAGE score of 3 did not follow the upward trend on psychological test scores as much as much as expected (Table II). These males were significantly younger than any of the other groups of males (Schofield, 1988). When they were compared with an age-matched subset of the male CAGE 0 patients, the difference in the mean psychological test scores increased for the GHQ and the HAD, but the results did not reach significance. The difference in mean scores was +3.29 (from +1.26) for the GHQ, and +2.57 (from +2.53) for the HAD. There was a narrowing of the gap between the mean BDI scores from −0.49 to −0.29 (Schofield, 1988).

TABLE IV

CAGE score and mean and standard deviation of psychological test scores in male and female abstainers and non-abstainers

Sex	*Psychological test*	*CAGE score*	*Drinking status*	*Number*	*Psychological test score* *Mean*	*s.d.*
Male	GHQ	1–4	Non-abstainer	39	4.9	5.8[1]
		1–4	Abstainer	9	11.6	8.4[1]
	BDI	1–4	Non-abstainer	39	4.3	4.8
		1–4	Abstainer	9	9.4	10.4
	HAD	1–4	Non-abstainer	39	5.9	3.9
		1–4	Abstainer	9	7.9	6.2
Female	GHQ	1–4	Non-abstainer	6	9.8	8.6
		1–4	Abstainer	3	9.3	3.5
	BDI	1–4	Non-abstainer	6	9.7	8.4
		1–4	Abstainer	3	2.0	0
	HAD	1–4	Non-abstainer	6	9.3	4.1[2]
		1–4	Abstainer	3	4.7	1.5[2]

1. $s.e._{diff} = 2.93$, $t = 2.28$, d.f. $= 46$, $0.05 > P > 0.02$.
2. $s.e._{diff} = 1.9$, $t = 2.45$, d.f. $= 7$, $0.05 > P > 0.02$.

It had been noted that the higher the CAGE score, the more likely it was that the patient had abstained from alcohol for at least one year. It was hypothesised that, since the higher the CAGE score the greater was the psychiatric morbidity, abstainers would have greater psychiatric morbidity than drinkers.

Totally-abstaining CAGE-positive men reported more morbidity than drinkers, significantly so on the GHQ. The converse is true of women, significantly so on the HAD (Table IV).

There was no significant difference in psychiatric morbidity between CAGE 0 drinkers (73 males and 69 females) and abstainers (6 males and 8 females) and non-drinkers (18 males and 34 females), neither for males nor females.

Discussion

The CAGE questionnaire has been used in this study to distinguish problem drinkers (see definitions in method section) from those without an alcohol problem. As the cut-off point for alcoholism in the CAGE questionnaire is usually set at 2/3, most of these problem drinkers would not be diagnosed alcoholic. Their scoring positively on the CAGE does not mean that they are necessarily progressing towards severe problems and presentation to the services. Many simply outgrow the problem. It can be seen that in this general-hospital sample, impaired psychological health is strongly associated with problem drinking. Those without a drink problem were much more likely to have, on average, lower levels of psychiatric morbidity. The questions raised by the low scores of those answering only one question positively on the CAGE are considered below.

The psychological tests used for this study were used as estimators and indicators of morbidity, and not as screening instruments (Goldberg, 1972; Tarnopolsky *et al*, 1979). No cut-off point was employed. The majority of these patients would not qualify as 'cases'. The study deals with the possible prodromal psychological changes induced by problem drinking as indicated by a positive CAGE score.

The scores of the GHQ, BDI and HAD tended to increase and decrease together. These questionnaires may be measuring aspects of the same psychological states which have not yet differentiated into the well known clinical entities of anxiety, depression etc. This would correspond to "that common core of non-specific symptoms of dysphoria and psychophysiological discomfort which characterises the hinterland between psychological illness and health" (Goldberg, 1981).

The males showed increasing psychological morbidity with increasing CAGE score. The dip in psychological test scores for the male CAGE 3 scorers is probably a function of the relative youth of this group of patients. This implies that the level of psychiatric morbidity in problem drinkers depends not only on the level of consumption as indicated by the CAGE, but also on the length of drinking history as indicated by the age of the patient. Some support for this hypothesis is found in the correlations of age and test scores (e.g. male CAGE 3 scorers: age and GHQ score, $r = +0.85$, $0.01 > P > 0.001$ (Schofield, 1988)).

The apparent superiority in psychological health, as indicated by the lower mean test score, of male CAGE 1 scorers over CAGE 0 and CAGE 2, 3 and 4 scorers is a rather surprising finding. The CAGE 1 scorers were not significantly younger than the CAGE 0, 2 and 4 scorers. Also, the finding is not due to the ratio of abstainers to non-abstainers in the CAGE 1 and CAGE 2 groups: of the 22 CAGE 1 males and 13 CAGE 2 males who took the psychological tests, three (14%) and one (8%) respectively were abstainers. It seems unlikely that the CAGE 1 men were psychologically healthier than those from the other CAGE groups, since they were concerned about their drinking, either feeling guilty about it or feeling that they should cut down on their intake as indicated by questions 1 and 3 on the CAGE, the two questions most likely to be answered positively by this group of problem drinkers (Schofield, 1988).

The finding that abstainers have high levels of psychiatric morbidity may suggest that not only does alcohol have a well known dysphoriant effect in heavy drinkers, especially marked on withdrawal, but also a 'semi-permanent' euphoriant effect most marked in the early, pre-alcoholic stage of drinking. It could be speculated that this euphoriant effect would be increasingly sought as the dysphoriant effects take hold, thus driving the drinker to greater consumption of alcohol.

This finding that abstainers have greater psychological morbidity than drinkers is supported by the findings of Wellman (1954), who reported late withdrawal symptoms, and DeSoto *et al* (1985), who showed that alcoholics attending Alcoholics Anonymous (AA) had psychological symptoms (most frequently depression) for up to ten years after cessation of drinking. The latter study also showed that among abstaining alcoholics attending AA, females had lower levels of depression and anxiety than males who had been abstaining for the same length of time, and this finding is supported by the results of this study.

It might be thought that cessation of drinking only reveals the basic personality structure and functioning which caused the alcoholism in the first place. However, Vaillant (1980) has shown that the personality of the alcoholic develops as it does because of the heavy drinking and that the basic personality cannot be distinguished as the cause of the alcoholism. This finding supports the idea that alcohol has a euphoriant effect which disappears on cessation of drinking, leaving behind the more lasting effect of dysphoria.

Research into the euphoriant effects of alcohol might distinguish between those people who have a propensity to this effect and those who have not, and so enable the biochemical factors which predispose towards the development of this addiction to be defined. The differing findings for men and women are especially interesting in this regard.

In conclusion, the results of this study suggest that further research is needed to determine whether the treatment of any clinical anxiety or depression found on cessation of drinking would help to prevent either chronicity or the temptation to relapse into the drinking state. For those working in liaison psychiatry in the general hospital, the necessity of an inquiry into the drinking habits of referred patients is underlined. In surveys of the psychological health of hospital in-patients (and probably other sections of the general population), alcohol consumption may be a major factor contributing to the levels of psychiatric morbidity.

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References

Beck, A. T. & Beck, R. W. (1972) Screening depressed patients in family practice. *Postgraduate Medicine*, **52**, 81–85.

DeSoto, C. B., O'Donnell, W., Alfred, L. J., *et al* (1985) Symptomatology in alcoholics at various stages of abstinence. *Alcoholism*, **9**, 505–512.

Ewing, J. A. (1984) Detecting alcoholism: the CAGE questionnaire. *Journal of the American Medical Association*, **252**, 1905–1907.

Goldberg, D. (1972) *The Detection of Psychiatric Illness by Questionnaire*. London: Oxford University Press.

—— (1981) Estimating the prevalence of psychiatric disorder from the results of a screening test. In *What is a Case?* (eds J. K. Wing, P. Bebbington & L. N. Robins). London: Grant McIntyre.

Jarman, C. M. B. & Kellett, J. M. (1979) Alcoholism in the general hospital. *British Medical Journal*, *ii*, 469–472.

Mayou, R. & Hawton, K. (1986) Psychiatric disorder in the general hospital. *British Journal of Psychiatry*, **149**, 172–190.

McIntosh, I. D. (1982) Alcohol-related disabilities in general hospital patients: a critical assessment of the evidence. *International Journal of Addiction*, **17**, 609–639.

Schofield, A. (1988) The CAGE questionnaire and psychological health. *British Journal of Addiction*, **83**, 761–764.

Tarnopolsky, A., Hand, D. J. McLean, E. K., *et al* (1979) Validity and uses of a screening questionnaire in the community. *British Journal of Psychiatry*, **134**, 508–515.

Vaillant, G. E. (1980) Natural history of male psychological health: VIII. Antecedents of alcoholism and orality. *American Journal of Psychiatry*, **137**, 181–186.

Wellman, M. (1954) The late withdrawal symptoms of alcoholic addiction. *Canadian Medical Association Journal*, **70**, 526–529.

Zigmond, A. S. & Snaith, R. P. (1983) The hospital anxiety and depression scale. *Acta Psychiatrica Scandinavica*, **67**, 361–370.

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Resettlement of Old Long-Stay Psychiatric Patients: the Use of the Private Sector

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A follow-up study of 17 old long-stay psychiatric patients resettled in private facilities for the elderly is reported. Resident satisfaction with the placement and functioning (using the CAPE Behaviour Rating Scale) was assessed, together with the quality of the physical and social environment, and the regime characteristics in the establishments. All residents were satisfied with life and their functioning had improved significantly. The private facilities were more resident-orientated, and had a generally superior social environment to their local authority 'old people's home' counterparts. The physical amenities, safety features, and architectural choice available were of a similar standard to those in local authority old people's homes, but there were fewer prosthetic and orientational aids and on-site recreational amenities.

There is a developing literature reporting varied outcomes following resettlement of old long-stay psychiatric patients (e.g. Farkas *et al*, 1987; Harding *et al*, 1987 *a*, *b*); however, this generally relates to large groups of people placed in a variety of community facilities. There has been little research into the use of specific types of accommodation, especially residential homes. Linn *et al* (1985) investigated the use of nursing home accommodation for the resettlement of psychiatric patients in the USA, and found that residents fared considerably worse in these on a variety of dimensions than did people in hospital wards. However, there are many ways in which nursing homes in the USA differ from residential homes in the UK, and thus direct comparisons of the two are probably unwise. For example, the average size of nursing homes in the Linn *et al* (1985) study was 120 beds, a great deal larger than private residential homes for the elderly in the UK, which usually house 8–20 residents, or local authority Part III establishments (i.e. local authority old people's homes), which typically house 40–50 residents (Willcocks *et al*, 1986).

In the UK, the most popular alternative to traditional care for old long-stay psychiatric patients has probably been the 'group home' (Ryan, 1979; Morris, 1981), but this type of relatively independent, communal living places high demands in terms of both skills and motivation, and is not appropriate for many of the more disabled residents (Shepherd, 1984). For those who lack the necessary skills and motivation for group home living, more supervised and supported accommodation is necessary. Often this is provided by long-stay hostels run by local authorities and voluntary bodies, or local authority Part III establishments for the elderly, but there are problems. In particular, there is a large shortfall in the number of places available in such accommodation, but there are other difficulties.

The first of these is that many Part III establishments are large and institutional in nature and practices (Willcocks *et al*, 1986). Of the 100 local authority old people's homes surveyed by Willcocks *et al* (1986), 68% had more than 40 residents, and 20% more than 50.

Secondly, many of the residents of Part III accommodation have disabilities of different types from those of long-stay psychiatric patients. In particular, many are disorientated and confused, and the environment is tailored to their needs rather than to the particular disabilities of long-stay patients, who often remain cognitively intact although still in need of a high level of support.

Thirdly, there are geographical limitations on placement in long-stay hostels and Part III accommodation, which often means that people are resettled in a place which is less than ideal for either themselves or their relatives. The catchment-area organisation of local authority accommodation of both types means that people may have to return to their borough of origin, despite the fact that decades spent in hospital mean that they no longer have any contacts there. Further, it is usually not possible to resettle people in groups or with friends they have made in hospital, who often originate from different boroughs. Although free from catchment-area constraints, voluntary hostels are not available in all areas of the UK, thus again the geographical choice is limited, and people are often resettled many miles from their previous homes and from any remaining relatives and social contacts.

Thus the available Part III and long-stay hostel accommodation offers limited choice and flexibility for resettlement purposes. This, together with the shortage of places available, has led many to turn to the private sector. This sector is rapidly expanding as a result of the Department of Health and Social Security (DHSS) system of payments for residential care, which make the provision of residential homes an attractive business proposition. In consequence there is a wide variety of small private establishments available in most areas of the UK. These fall broadly into two categories: 'residential homes for the elderly', and 'very small homes'.

Residential homes for the elderly are small establishments (usually housing 8–15 people) and usually consist of large old houses, staffed and converted in line with local authority registration requirements. Despite the relative uniformity of these registration requirements, such homes are very varied in standards, practices and client group served. Some cater for more able elderly people, others take more confused and dementing residents. Often such establishments are run by nurses experienced in the care of the mentally ill.

'Very small homes' are homes housing three people or less and are therefore not liable for registration with the local authority. They are generally run in ordinary houses, with owners living either on the premises or nearby. In order to attract DHSS residential care payments they must satisfy the conditions laid down in the DHSS letter of August 1987 entitled "Supplementary benefit: very small homes". These regulations require, for example, that at least two responsible people, with at least one year's experience of caring for the relevant client group, are engaged in care duties; that at least one such responsible person is on duty throughout the day and night; and that residents have unrestricted access to the home at all times. Such homes must be distinguished from 'supportive lodgings', which do not offer 24-hour staffing or such a high level of input (and thereby attract a much lower level of DHSS payment).

There are clearly advantages and disadvantages with the use of private accommodation, but with the pressure to reduce the number of long-stay hospital residents, such facilities appear to represent an extensively used but underinvestigated resource.

The purpose of this study was to monitor and evaluate the initial success, or otherwise, of placing old long-stay psychiatric patients from a large London teaching hospital in private facilities. Most of these people were resident in a large old long-stay unit of the hospital which it is hoped will close soon, with limited community developments for residents currently planned. Thus the available options for the majority were either resettlement in existing accommodation in the community, or return to the main hospital. In the light of the extreme shortage of suitable voluntary or statutory provision in the area, for many the private sector was the only option.

Method

Subjects

Seventeen old long-stay hospital residents (seven men and ten women) who had been resettled in private residential homes for the elderly or 'very small homes' were the subjects in this study. Their mean age was 72.1 years (s.d. 7 years), and mean length of continuous hospital stay was 23.6 years (5–44 years).

Materials

Functioning of residents

The functioning level of the residents was assessed using the Behaviour Rating Scale of the Clifton Assessment Procedure for the Elderly (CAPE; Pattie & Gilleard, 1979). This scale provides a measure of an individual's level of behavioural disability and has been widely used to assess the functioning level of elderly psychiatric and psychogeriatric patients. The rating scale is completed by an observer familiar with the subject's behaviour, and provides a measure of four principal areas: physical disability (Pd), apathy (Ap), communication difficulties (Cd), and social disturbance (Sd).

Quality of the physical and social environment

The quality of the physical and social environments in each of the homes used was investigated using measures developed by Willcocks *et al* (1986) in their similar, but much larger, cross-sectional National Consumer Survey of 100 public sector residential homes. This measure was used as it was considered important that the quality of private care should be compared with that available in the equivalent, non-psychiatric, public (local authority) sector facilities, and not with the hospital care that all residents had previously experienced. This was done because, if community care and resettlement are to present positive advantages for people with psychiatric disabilities, it is not sufficient to take the poor practices and facilities obtaining in most old long-stay areas of large psychiatric hospitals as the point of comparison. The scale considers four dimensions of the social environment that research has shown to be important.

(a) choice/freedom: the degree to which residents have a choice or degree of freedom over their lifestyle; e.g. meal times, going out, getting up
(b) privacy: the availability of privacy, both personal and in interactions with others
(c) involvement: degree of resident participation in the organisation of home life, and their knowledge concerning how the home is run
(d) engagement/stimulation: the degree to which staff encourage resident autonomy and independence.

In terms of the physical environment, scales developed by Willcocks *et al* (1986) were employed to assess the following key dimensions.

(a) physical amenities: those features of the environment which add to convenience or increase comfort; e.g. toilets within 10 metres of lounges and dining rooms; bedside lights
(b) social/recreational aids: facilities which encourage recreational activities or increase social interaction; e.g. more than one television; chairs in the entrance hall
(c) prosthetic and orientational aids: aspects of the physical environment that enable residents to negotiate the setting and carry out activities of daily living without unnecessary dependence on staff; e.g. WCs that will accommodate wheelchairs; noticeboards
(d) safety features; e.g. call systems
(e) architectural choice: features of the environment that allow control and choice; e.g. control over bedroom heating; windows that open.

These scales were completed by a senior staff member in the home. High scores indicate a more progressive style of organisation and social environment within the home, with an emphasis on residents being treated as individuals with some control over their lives, and a high level of physical amenities.

Regime characteristics

In order to offer an overall assessment of the characteristics of the regime in the home, two further scales developed by Willcocks *et al* (1986) were employed: resident-oriented practices (those aspects of the physical and social environment designed to facilitate resident actions), and staff-oriented practices (those aspects of the physical and social environment designed to facilitate staff actions). High scores indicate a high level of facilities in each domain.

Resident satisfaction with life at the home

Resident satisfaction was assessed by interviewing residents using an adaptation of parts of a schedule developed by Willcocks *et al* (1986). This involved the following components:

(a) overall satisfaction with life in the new environment, measured on a four-point scale, from very satisfied; this was compared with a retrospective judgement concerning satisfaction with life at the hospital on the same scale, and a question concerning whether or not the person would like to return to the hospital
(b) satisfaction with staff, assessed by a series of questions concerning the person's satisfaction with interactions with staff
(c) adjustment to home life, measured by a series of items concerning how easy the person found adapting to life at the home when they first moved in
(d) worries about aspects of home life.

Procedure

Prior to all resettlement plans, all residents at the long-stay unit were assessed using the CAPE Behaviour Rating Scale. This scale was administered by a senior nurse from outside the unit on the basis of information gained from the staff working there. For all those residents who had been resettled in private facilities, a follow-up survey was conducted in which a psychologist interviewed each of the residents using the modified Willcocks *et al* (1986) instrument designed to assess satisfaction with home life. All interviews were conducted in private and the residents were informed that their replies would be confidential. A social worker, trained in the use of the instruments, completed the CAPE Behaviour Rating Scale for each resident in conjunction with staff at each home. The questionnaires concerning quality of the social and physical environments and regime characteristics were completed, in the manner described by Willcocks *et al* (1986), by senior staff at the home assisted by a social worker.

Results

Placements

Of the 17 people resettled, 12 (70%) had been placed in five private residential homes for the elderly, and the remaining 5 in three 'very small homes'; 13 (77%) had been placed within small groups of people whom they knew from the hospital, and four had been placed alone. At the time of the follow-up, residents had been living in their new community accommodation from 1 month to 13 months.

Satisfaction with the placement

Twelve of the residents said that they were very satisfied with life in their new homes, and the remainder were "fairly satisfied". No one was "not very satisfied" or "not at all satisfied". None of the 17 residents said that they wanted to return to the hospital: four said that they were equally satisfied with life in their new accommodation as they had been in hospital, and the remainder (76%) said that they were more satisfied with life in their new accommodation. The reported satisfaction of those who had been in their new accommodation for some time and those who had only recently moved in did not differ.

Thus, all residents were satisfied with their new homes and wanted to remain, and most preferred life there to life in hospital.

Resident functioning

The CAPE Behaviour Rating Scale scores of residents can be seen in Table I. The total scores before and after resettlement, and scores in the four principal areas, were compared using Wilcoxon test statistics. The comparison showed a significant decrease in total Behaviour Rating Scale scores, indicating an overall decrease in disability level ($T = -18$, $P < 0.05$). There was no significant change in scores in the areas of communication difficulties and social disturbance, but there was a highly significant decrease in apathy scores ($T = -12$, $P < 0.01$), and a decrease in physical disability scores ($T = -18$, $P < 0.05$).

TABLE I

CAPE Behaviour Rating Scale scores before resettlement and at follow-up ($n=17$)

	Before resettlement		*At follow-up*		*Wilcoxon* T
	Mean	s.d.	Mean	s.d.	
Age: years			72.1	(7.0)	–
Length of hospital stay: years	23.6	(14.3)	–	–	–
Total Behaviour Rating Scale score	8.8	(6.1)	5.6	(4.0)	$T=-18^*$
Physical disability (Pd) score	2.7	(2.9)	1.4	(1.7)	$T=-18^*$
Apathy (Ap) score	5.2	(3.5)	3.7	(2.5)	$T=-12^{**}$
Communication difficulties (Cd) score	0.1	(0.5)	0.3	(0.6)	$T=-54$
Social disturbance (Sd) score	1.1	(1.7)	0.6	(1.1)	$T=31.5$

$^*P<0.05$; $^{**}P<0.01$.

This indicates that most of the improvement in overall functioning could be accounted for by a substantial improvement in residents' constructive engagement with, and involvement in, their environment, and a decrease in the input they required for bathing, dressing, going out, etc.

In order to check that a 'honeymoon effect' in those who had only recently moved did not unduly bias these findings, the changes in CAPE Behaviour Rating Scale scores of those who had been resettled for some time and those who had only recently moved were compared. There was no significant difference in the changes in scores of these two groups ($U=19$, $P<0.05$).

Quality of the social environment

Scores on the four scales relating to the social environment were compared with those obtained in the Willcocks *et al* (1986) study of a representative sample of 100 local authority old people's homes. This was achieved by converting the scores for each of the private establishments into z scores using the means and standard deviations obtained in the Willcocks *et al* study.

These scores showed that the quality of the social environment in each of the private homes used was higher than that found in the average local authority old people's home: in all areas the average score of the private homes used was at least one standard deviation higher than that of their statutory counterparts. In comparison with local authority homes, the private facilities used scored, on average, 1.7 standard deviations higher on the 'choice/freedom' scale (range 0.7–2.2), 1.4 standard deviations higher on the 'privacy' scale (range 0.8–1.8), 1.0 standard deviations higher on the 'involvement' scale (range 0.2–1.5) and 3.0 standard deviations higher on the 'engagement/stimulation' scale (range 1.6–3.4). In particular, these scores indicate that the average engagement score (the degree to which resident autonomy and independence were encouraged) was equivalent to that of the best 1% of local authority homes, and the average choice/freedom score (the extent to which residents had choice/freedom over their own lifestyles) was equivalent to that of the best 5% of local authority homes.

Thus it is clear that the quality of the social environment in the private homes used was superior to that found in most local authority old people's homes: residents had greater choice/freedom, more privacy, and a greater involvement in the organisation of home life, and were encouraged towards greater autonomy and independence.

Quality of the physical environment

Scores in the areas of physical environment assessed were also converted to z scores to permit comparison with the standards obtaining in the local authority old people's homes in the Willcocks *et al* (1986) study.

In comparison with local authority homes, the private facilities used scored, on average, 0.9 standard deviations higher on the 'physical amenities' scale (range 0.2–1.6), 0.5 standard deviations higher on the 'architectural choice' scale (range −0.4–1.0), and 0.2 standard deviations higher on the 'safety features' scale (range −1.5–1.8). However, the private homes scored lower than the local autority homes on the 'prosthetic aids' scale (mean z score −2.4, range −4.3 – 0.4), the 'orientation aids' scale (mean z score −0.9, range −1.8 – 0.2) and the 'social/recreational amenities' scale (mean z score −0.3, range −1.0 – 1.7).

This suggests that, whereas the physical amenities, architectural choice (features that allow the individual control and choice), and safety features were of a similar standard to those found in most local authority homes, there were generally fewer prosthetic and orientational aids and social/recreational amenities provided on site. The private facilities were not, in general, equipped with lifts, handrails, specially converted WCs, signs, colour-coded routes, on-site bars, recreational rooms, etc.

Regime characteristics

The scores on scales relating to resident- and staff-oriented features of home life were converted to z scores in the manner described previously, to allow comparison with those found in local authority old people's homes. This indicated that the private homes were more resident-oriented than their local authority counterparts (mean z score for resident-oriented policies scale 1.3, range 0.15 – 1.9), and had lower levels of staff-oriented policies (mean z score – 1.8, range – 1.4 to – 2.2). Thus it appears that the private facilities had more aspects of the physical and social environment designed to facilitate resident actions, and fewer designed to facilitate staff actions, than the local authority homes: they were more resident-oriented environments.

Discussion

This follow-up study clearly showed that the old long-stay residents resettled in private accommodation were all at least equally satisfied with life in their new homes as they had been with life in hospital, and none wanted to return to hospital. Although not directly comparable in this context because of the different previous accommodation of the subjects, the Willcocks *et al* (1986) study found that only 45% of the 1000 residents of local authority old people's homes interviewed maintained the same level of satisfaction before and after their move. The high level of satisfaction is gratifying given that all but two of the people resettled were reluctant to leave hospital: they were not a group who were highly motivated to leave and had the unit not been designated for closure, many may well have remained in hospital unnecessarily.

Not only did residents express satisfaction with their new surroundings, their functioning, as measured by the CAPE Behaviour Rating Scale, improved significantly. As might be expected with a group such as this, communication difficulties and social disability scores remained static despite resettlement; however, it is particularly interesting that their apathy scores decreased dramatically. This is particularly important in the light of some of the problems that have been experienced with the use of group homes for old long-stay hospital residents. Ryan (1979) found that with inadequate supervision underactivity in group homes was a major problem.

The significant decrease in physical disability scores was rather surprising, but probably resulted from a decrease in staff input in such areas as bathing, dressing and going out, resulting from the private facilities' emphasis on individually tailored care. In the hospital unit where most of the sample had been living, block treatment was prevalent, and, for example, the routine required that everyone be supervised while having a bath, irrespective of their needs.

Any conclusions drawn from the present data must be cautious in the light of the small sample size, and short and variable length of follow-up. Clearly, longer-term follow-up would be desirable, but clinical experience suggests that a high proportion of unsuccessful placements break down in their initial stages. The short-term results are promising and suggest that further exploration of this type of facility would be worthwhile. The results obtained here are quite different from those of Linn *et al* (1985), who found private nursing home accommodation in the USA to be a less desirable alternative to hospital admission in terms of resident satisfaction and functioning. The studies are not directly comparable in terms of their methodology and client group considered (the Linn *et al* study involved a considerably younger group of patients, with a mean age of 62.6 years, a large proportion of whom suffered from organic brain syndrome). Nevertheless, the marked difference in results does suggest that UK private residential accommodation for the elderly is not comparable with US nursing home accommodation, and may represent a desirable alternative to hospital admission for old long-stay psychiatric patients.

Turning to the homes themselves, the quality of the social environment within them is superior to that found in most local authority old people's homes–the statutory alternative for elderly people in need of sheltered and supported accommodation. People in smaller private accommodation had greater choice about their lifestyle and privacy, were more involved in the running of the home, and were encouraged to a greater degree of autonomy and independence than they probably would have experienced if they had been placed in Part III accommodation (and certainly greater than they experienced in hospital). In addition, the policies in the homes used were more resident-oriented and less staff-oriented than those in most similar local authority establishments, or in hospital: the social and physical environment was designed to facilitate resident, rather than staff, actions.

In terms of the physical environment in the private facilities, the physical amenities, safety features, and architectural choice were at least comparable with those found in most similar local authority provision, but there were fewer prosthetic and orientational aids available, and fewer on-site social/recreational aids. This is probably a reflection of the more domestic style of the accommodation: there may be a 'trade-off' between the introduction of such aids and the domesticity and normality of the environment. This would mean that such private establishments are relatively unsuitable for people with needs in these areas.

This study does not purport to offer a representative picture of the social and physical environments in private facilities. The establishments used in this study were vetted and selected before resettlement was considered, and several potential places were rejected. Instead, these data probably reflect what can be found in the private sector, rather than what is typical of that sector. The possibility of such selectivity is a key feature of the private sector: there is a greater range of choice available in the current financial climate than pertains in the statutory domain.

Despite the apparent advantages of private facilities, the potential problems associated with their use must not be underestimated. Their quality is variable, and careful assessment and selectivity is required. They have no statutory obligation to continue to provide care: although standards are monitored, there is nothing to prevent private facilities going out of business. Finally, the use of DHSS funding is a matter of concern. Currently rates are high enough to make such homes a viable economic proposition for their owners. However, if there are changes in the system, or the benefit level drops in real terms, then the placements could be in jeopardy. Continued monitoring and follow-up on the part of the resettling team is therefore essential. It is critical that the resettling team, or some other statutory group, undertake indefinite monitoring and follow-up of residents resettled in such facilities, and that careful resettlement plans are made.

In the resettlement process described here a detailed follow-up and continuing care plan for each resident was drawn up prior to discharge. This included specification of a continuing care key-worker (from among the team who was looking after the person in hospital) and specification of the minimum frequency with which the person had to be visited. The team is committed to long-term follow-up and support without limit of time. Intensive, and indefinite, follow-up of this sort is necessary given the non-statutory nature of the placements and the degree of support and advice that the staff of the private facilities require (from difficulties with the DHSS to individuals' behavioural problems). The continuing cost and staffing implications of this must not be underestimated, but current results indicate that private homes for the elderly are a resource that cannot be ignored.

References

Farkas, M. D., Rogers, E. S. & Thurer, S. (1987) Rehabilitation outcome of long-term hospital patients left behind by deinstitutionalisation. *Hospital and Community Psychiatry*, **38**, 864–870.

Harding, C. M., Brooks, G. W., Ashikaga, T., *et al* (1987*a*) The Vermont longitudinal study of persons with severe mental illness: I. Methodology, study sample and overall current status. *American Journal of Psychiatry*, **144**, 718–726.

——, ——, ——, *et al* (1987*b*) The Vermont longitudinal study of persons with severe mental illness: II. Long term outcome of subjects who once met criteria for DSM III schizophrenia. *American Journal of Psychiatry*, **144**, 727–735.

Linn, M. W., Gurel, L., Williford, W. O., *et al* (1985) Nursing home care as an alternative to psychiatric hospitalisation. *Archives of General Psychiatry*, **42**, 544–551.

Morris, B. (1981) Residential units. In *Handbook of Psychiatric Rehabilitation Practice* (eds J. K. Wing & B. Morris). Oxford: Oxford University Press.

Pattie, A. H. & Gilleard, C. J. (1979) *Manual of the Clifton Assessment Procedures for the Elderly (CAPE)*. Sevenoaks: Hodder & Stoughton.

Ryan, P. (1979) Residential care for the mentally disabled. In *Community Care for the Mentally Disabled* (eds J. K. Wing & R. Olsen). Oxford: Oxford University Press.

Shepherd, G. (1984) *Institutional Care and Rehabilitation*. London: Longman Applied Psychology.

Willcocks, D., Peace, S. & Kellaher, L. (1986) *Private Lives in Public Places*. London: Tavistock.

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Signal and Noise in Psychotherapy
The Role and Control of Non-specific Factors

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Four major categories of non-specific or common factors are systematically analysed: relationship, expectancy, reorganising, and impact factors. The placebo control method should be discarded in psychotherapy research for two reasons: (a) sham treatment controls are unworkable because common factors in treatment are manifest only when real treatment is administered; and (b) the very events which were once thought of as 'non-specific' noise are now recognised as active therapeutic factors common to many schools.

Psychotherapy never seems to merit unambiguous status. The best testimony to its value is still met with doubts about its uniqueness, its effectiveness, or its scientific basis (Brody, 1983; Prioleau *et al* 1983; Shepherd, 1983). The latest doubts spring from students of so-called non-specific factors in therapy. The term 'non-specific factors' has been charged with excessive ambiguity, and alternative terms, such as 'common factors', have been proposed instead (Critelli & Neumann, 1984). We mostly use the original term, however, to mean factors which are not exclusive to a particular therapy.

Interest in this topic originated independently from Jerome Frank's astute comparisons of psychotherapy with folk traditions of healing (Frank, 1961, 1973), and from the methodology of random clinical trials drug research which, applied to psychotherapy, equated non-specific factors with placebo effects (Rosenthal & Frank, 1956). This interest has increased research sophisticiation, but at some cost. It has led to some erroneous debunking of psychotherapy as an effective means of treatment, and to a gratuitous devaluation of the non-specific factors themselves as treatment devices. It has also caused the proliferation of wasted research funds in the pursuit of a methodological chimera – the 'non-treatment' or 'placebo' control. This paper aims to correct these errors.

The attack on psychotherapy via non-specific factors is based on two flawed arguments. The first is the notion that only factors specific to a therapy require scientific inquiry. Non-specific factors, this says, are not derived from any treatment theory and therefore should play only an ancillary role to specific factors in treatment. The second argument says that a treatment's efficacy depends on its outcome test results against a placebo control using non-specific factors only. This paradigm assumes that non-specific factors can be separated from specific factors and applied without an accompanying specific technique (the independence assumption). Some critics conclude from research with this paradigm that all therapeutic effects are placebo in nature (Prioleau *et al* 1983), or that treatment outcome depends so much on placebo effects that psychotherapy does not require professional training (Brody, 1983).

The overvaluation of specific effects and the unrealistic methodology that comes from it are both relics of a previous era, dominated by sectarian claims of therapy schools to having uniquely effective methods. Interest in non-specific factors, on the other hand, has gone through several historical phases. In the first, only specific factors were deemed important to treatment. Non-specific factors were to be filtered out by placebo controls (Rosenthal & Frank, 1956). Then, non-specific factors were recognised as crucial to both psychotherapy and traditional healing (Frank, 1961). Next, non-specific factors were 'professionalised', that is, they became intentional elements of treatments that had once neglected them, and therapists were explicitly trained in them (Strong & Claiborn, 1982; Patterson, 1985; Karasu, 1986; Omer, 1986, 1987). Now, placebo controls are coming to be seen as irrelevant to evaluation of psychotherapy's efficacy, since non-specific factors are not noise to be filtered out of 'real' treatment, but are important signal events in it. Some who take this position argue that non-specific factors *should not* be controlled for in efficacy studies (Kirsch, 1978; Wilkins, 1979, 1983; Parloff, 1985; Horvath, 1987). Our analysis goes a step further and argues that no-treatment or sham-treatment groups *cannot* serve as adequate controls for efficacy tests.

Our analysis of the literature on four major groups of non-specific factors in psychotherapy (relationship, expectancy, reorganising, and impact factors) shows in each case that the independence assumption is unwarranted, that sham-treatment controls are inadequate, and that non-specific factors function as important signals, not as noise, in the process of psychotherapy. In fact, understanding the non-specific factors offers improved therapeutic technique, new theories linking psychotherapy to social and cognitive psychology (Bandura, 1977; Strong & Claiborn, 1982), and greater dialogue between schools (Goldfried, 1980).

Relationship factors

The development of a special relationship between therapist and client is a common feature of all psychotherapies. It is often seen as a major therapeutic factor in itself, if not the only vital one. Attention-placebo groups are attempts to control for the relationship factor by providing the benefits of a therapeutic relationship without any treatment.

In attention-placebo groups, control clients are given equal therapist *time* in sessions where the actual contents of the interaction are supposedly non-therapeutic. The validity of this control depends on how well the therapist's attention alone represents the therapeutic relationship. Critical scrutiny of three major relationship factors, however, suggests that it depends on specific interventions and is not manifest without them.

(a) *The unconditionally positive relationship.* Contemporary 'experiential' psychotherapy makes the relationship the central vehicle of therapeutic change. It heals by providing a secure atmosphere in which the client is accepted as is, which leads to abandoning the defences which thwart growth and self-revelation (Barton, 1974). The relationship should be free of the therapist's direction or content preferences, and the therapist should be empathic, warm, and genuine. There is evidence that these therapist traits are helpful in all treatments, not just in experiential psychotherapy (Patterson, 1985). If these treatments were indeed non-directive, they might themselves be ideal control groups for therapist attention. But they are not: experiential psychotherapists differentially encourage one or another kind of client behaviour, such as 'introspective feeling' statements (Murray & Jacobson, 1971). In short, the unconditional positive relationship becomes manifest only through specific interventions. Administering sham treatments cannot replace specific interventions because this precludes therapist genuineness. Attention-placebo groups cannot therefore control for the positive effects attributed to a warm and empathic relationship.

(b) *Relationship as vehicle for identification and modelling.* Another view of the therapeutic relationship as a healing factor sees the therapist as a model for the client to imitate or identify with (Frank, 1973, pp. 127–130; Cornsweet, 1983). What is modelled differs from therapy to therapy, but it is generally agreed that therapist models need to be unambiguous (Cornsweet 1983; Messer, 1986). Placebo groups cannot easily control for this non-specific factor, since a faking therapist will probably be less convincing and invite less identification than a genuine one.

(c) *Relationship as therapist power.* Some theorists argue that the seemingly undemanding therapist manner is a means of creating a power differential in the therapist's favour (Haley, 1963; Strong & Claiborn, 1982). Such power is not crude dominance over the client's life, but the capacity to define the roles and rules of the therapeutic encounter (Haley, 1963) and to foster the clients' perception that therapists have the resources to meet their needs (Strong & Claiborn, 1982). Power differential is common to all treatments and is used in ways that cannot be matched by placebo controls. The therapist may, for instance, use control of the relationship to press the client to perform difficult or frightening tasks, such as freely associating or approaching a phobic object, or to make sure that the client will not dismiss a paradoxical intervention out of hand (Haley, 1963; Strong & Claiborn, 1982). Power differential can be used this way when the therapist has clear interventions in mind. Invoking it for irrelevant purposes, however, as in sham therapy, may actually weaken the therapist's power.

In summary, all three relationship factors, contrary to the independence assumption, become manifest only through real specific interventions and cannot be controlled for by groups receiving no (or sham) treatment attention.

Expectancy effects

Expectancy effects occur because clients and therapists expect treatment to be helpful, independently of the specific stratagems used. Expectancy effects are generally recognised as important factors in all treatments (Frank, 1973, pp. 136–164; Shapiro & Morris, 1978). 'Expectancy groups' in which subjects receive a 'highly credible' sham treatment (Borkovec & Nau, 1972) try to control for these effects: in the treatment group, it is thought, outcome will depend on both treatment and expectancy; in the control group, it should be due to expectancies alone. The 'expectancy arousal hypothesis' says that *all* therapy effects are merely expectancy ones (Shapiro, 1981). Convincing expectancy control groups are virtually impossible to construct, however, and evidence for the expectancy arousal hypothesis is flimsy.

Therapist expectancy effects

Therapists' positive attitudes towards the client and optimistic expectancies correlate positively with outcome (Goldstein, 1962, pp. 35–52; Frank, 1973, pp. 152–165; Shapiro & Morris, 1978). Therapists' negative expectancies, on the other hand, may neutralise the effect even of medical treatments known to be active (Uhlenhuth *et al*, 1966). Therapist expectancies about the length of therapy influence the rate of improvement as perceived by clients (Goldstein, 1962, pp. 76–84; Frank, 1973, pp. 158–159). Therapist expectancies interact with the quality of the therapeutic relationship: positive expectancies make the therapist more interested and involved and, therefore, lead to a warmer relationship, while negative expectancies lead to more detachment (Wallach & Strupp, 1960).

Therapist expectancies parallel teacher expectancies on pupils (Rosenthal, 1974; Harris & Rosenthal, 1985) and may work through parallel mechanisms. Teachers give preferential treatment to high-expectancy pupils in four ways: (a) more emotional support; (b) clearer and more favourable feedback; (c) more attention and more teaching; and (d) more opportunities to perform and learn difficult material. Teachers' differential behaviour may lead pupils to reciprocate (low-expectancy pupils, for instance, may react to teacher avoidance or it may lead pupils to accept the teacher's judgements (low-expectancy students may become convinced that they are no good). Expectancies, furthermore, lead to selective perception and interpretation of ambiguous information in a self-confirming manner, thus perpetuating a self-fulfilling prophecy (Jussim, 1986). The same mechanisms may apply to non-specific and specific psychotherapy factors (expectancies and actual tactics) and between different non-specific factors (expectancy and relationship factors). If positive expectancies are consistently linked to better therapy and vice versa (better therapy leading to higher therapist involvement and therefore to higher expectancies), it is hard to imagine how therapist expectancies could be isolated in a placebo group: therapists' attitudes and expectancies cannot be made comparable between real and bogus treatments. Maybe the only way of having highly positive expectancy therapists for bogus procedures is to commit them to a specific research outcome, such as support for the expectancy arousal hypothesis. The fact that sham-treatment groups cannot match real-treatment groups on therapist expectancies undermines their utility: if the treatment group proved superior, one could always argue that the control group was not matched on therapist expectancies. Only null effects (that is, no superiority of treatment groups) would then be convincing.

Expectancies related to treatment credibility

Treatment creates expectancies for change. In control conditions, therefore, clients must believe that they have been treated, and not just any treatment will do – some are more credible than others and therefore create higher expectancies (Borkovec & Nau, 1972). Shapiro (1981) showed that credibility ratings of various treatments paralleled their differential effectiveness. These findings were taken to support the expectancy arousal hypothesis, although Shapiro himself suggested as an alternative that clients are simply good at evaluating treatments' potential for helping them.

Kirsch (1985) reviewed a dozen studies comparing desensitisation to highly credible placebos and concluded that, since most of them did not find significant differences favouring desensitisation, the expectancy arousal hypothesis was supported. We disagree, because a no-difference conclusion needs support from tests of high statistical power. Samples in the studies Kirsch reviews are very small ($n = 8–12$ per cell), which makes for low power levels (power levels are the converse of significance levels (Cohen, 1969)). We should not expect significant effects in those studies. With the samples in the studies reviewed by Kirsch (1985) and assuming expected effects of moderate size (e.g. 0.5 s.d.), power ranges from 15% to 21%, which means that even if a real difference had been present, the chances of missing it were from 79% to 85%. This is a weak basis for a 'non-difference' verdict.

Support for the expectancy arousal hypothesis is further weakened by the fact that, in most of the studies reviewed, trends favoured desensitisation. This shows that sham-control studies may be fruitless either way: if significant results are obtained, one can *always* dismiss them by claiming that the control group was not credible enough, whereas a conclusion of no-difference demands power levels far beyond those achieved by existing studies on this topic. The fact that trends have usually favoured desensitisation should discourage anyone from attempting a large-scale study in order to support the null hypothesis. Placebo studies, in short, are not adequate for testing the expectancy arousal hypothesis.

Culturally determined expectancies

Acceptable and unacceptable treatments, patient–physician and therapist–client relationships are all culturally defined (Hahn, 1985). Culturally determined expectancies also influence therapeutic outcome and interact with other specific and non-specific factors. Therapist attitudes in the use of hypnotherapy among Israeli-born and Russian-born therapists in Israel, for instance, are typically different: the Israelis get their best results with permissive, open-ended suggestions, the Russians with an authoritarian approach. Different responses to prescribed medication also illustrate interactions between cultural norms and specific factors: for many native Israelis, a successful visit to a physician must produce a prescription, while Ethiopian immigrants often turn their prescribed pills into good-luck necklaces. When specific treatments combine with cultural backgrounds, both are transformed and new properties emerge. The combination of non-specific and specific factors, contrary to the independence assumption, is like a chemical compound, not a mixture.

Expectancies about the self

Expectancies about the self reflect our beliefs about how we will behave in different situations. Self-efficacy theory (Bandura, 1977) and, more recently, response expectancy theory (Kirsch, 1985) deal with this issue. An efficacy expectation is the belief that one can do what is required to achieve a desired outcome. Self-efficacy theory asserts that such convictions determine the initiation and persistence of coping behaviour (Bandura, 1977). Psychological treatments are means for developing self-efficacy expectancies via (in order of decreasing importance) successful performance, vicarious experience, verbal persuasion, and the information produced by one's own emotions. The relative effectiveness of a treatment depends on how much it makes use of which means.

Response expectancy theory deals with expectations about such involuntary responses as emotion and pain (Kirsch, 1985). Since such responses can be pleasant or unpleasant, people's expectations about them affects their readiness to do things which may elicit those feelings. Acrophobics, for instance, avoid high places because they expect to panic when reaching them. Response expectancies also have a self-fulfilling quality, increasing the probability that the expected responses will indeed occur: expecting a panic attack helps bring one about. Psychotherapy works, this theory says, by modifying response expectancies.

The two theories each explain both non-specific and specific effects of therapy: effects of 'real' treatment, persuasion, and bogus manipulation are all described by the same concepts. Desensitisation, for instance, works via either self-efficacy or response expectancies, as does any effective placebo or non-specific factor. For this reason, says Kirsch (1978), placebo groups have no place in psychotherapy research. In sum, expectancy factors are not peripheral events in psychotherapy to be filtered out by appropriate methodology: they are *bona fide* and major treatment factors.

Reorganising factors

There are other non-specific factors in psychotherapy which are less widely recognised and discussed than relationship and expectancy. The reason may be, in part, because therapy schools tend to describe them in the specialised language of their own theories, and therefore fail to recognise their common functions. Specific techniques often differ across schools. As is always true in psychotherapy, however, 'specific' often refers to techniques and 'non-specific' to the functions they achieve. The less recognised, non-specific factors are also less investigated in psychotherapy research, perhaps because procedures are lacking for simulating them in placebo-control groups. Three of them are: (a) dismantling clients' dysfunctional patterns (Pentony, 1982); (b) providing new perspectives and concepts (Parloff, 1986); and (c) helping the client to address problems differently.

(a) Dismantling dysfunctional patterns

All psychotherapies dismantle or 'unfreeze' dysfunctional patterns (Bennis *et al*, 1973; Pentony, 1982, pp. 9–14), chiefly by mobilising disaffection in the client about the patterns themselves, and by loosening and modifying the pattern's contextual supports.

Mobilising disaffection

Although clients usually come to therapy wanting to change, their motivation is often too weak or narrow to work. All therapies try to boost this motivation by playing upon the client's capacity for self-dissatisfaction. This helps to undermine clients' attachments to their old patterns. One common therapeutic means is by pointing out discrepancies between the undesired behaviour and the image clients hold of themselves as persons with integrity, autonomy, and goodness. Another is by highlighting potential dangers of their behaviour for themselves and others. A third is by uncovering the irrationality of their assumptions. A fourth is by reflecting contradictions in their statements and expressions of thought and feeling. There are yet others. By such means, guilt, anxiety, and displeasure are aroused and therapeutically channelled.

Loosening and modifying contextual supports

Symptom patterns are supported by the intrapersonal, social, and situational contexts in which they are embedded. Different theories stress different contextual links, such as family interactions, maladaptive cognitions, or reinforcement contingencies. Symptom patterns are thus parts in a jigsaw puzzle which is stabilised by its interlocking features. Psychotherapy tries to change the contextual props, to destabilise the puzzle by spoiling pieces' fit. Paradoxical interventions which figure in many kinds of therapy (sometimes by different names) dramatically illustrate this process by the absurd perspective they cast on the symptoms they address. Typically, the therapist prescribes intense repetitions of the very symptomatic behaviour about which the patient is complaining. Since the therapist's reaction and prescription are both foreign to the patient's expectations, the social and affective context is thereby shaken (Omer, 1986).

In different therapies, different choices are made about the contents and contexts they deal with, but all deliberately spoil the fit between symptom and context. Unfreezing is attempted equally in therapies which stress cognition, affect or behaviour. Specific techniques, if anything, are vehicles for conveying this non-specific factor.

(b) New perspectives and concepts

Therapies provide clients with a new view and a new rational account of their problems. This is often done in what is called a consciousness-raising process, in which the client becomes aware of previously unattended factors. Whether awareness *increases* is a moot point, but certainly the centre of attention shifts. Therapies also provide clients with new terminology, new ways of explaining events, and new conceptual schemes of the change process. Providing such organising schemata may be vital, regardless of their particulars, for allowing clients: to redefine and reframe problems; to provide an orderly account of their difficulties; and to conceptualise the change process.

Redefining and reframing

A new terminology not only relabels, but redefines and reframes the issues for the client. In learning to speak differently, clients are already changing their problems, possibly into more solvable ones. Redefinition also reframes the problem area by bringing in elements other than the ones originally attended to. A new cognitive map is thus created for facilitating alternative behaviour (Bennis *et al*, 1973).

Providing an orderly account

Conceptual schemata acquired in therapy order and simplify the chaotic diversity of events, by organising them into a rational, lawful-seeming framework. The accuracy of the organising hypotheses may be less important than the very fact that events are ordered and explained (Spence, 1982, pp. 175–214). A feeling of mastery and predictability thus replaces former helplessness.

Conceptualising change

The therapeutic scheme also conceptualises the change process itself through a change agent supposedly released in treatment which leads to a resolution of the problem. Strong & Claiborn (1982, p. 29) recommend that the change agent should be thought of as working inevitably and automatically, and as originating in the client and not in the therapist. Examples of such agents are organismic growth, basic rationality, released psychological energy, insight, and the Holy Spirit (Strong & Claiborn, 1982, p. 133). These constructs redirect the client's attention and foster optimism.

(c) Confronting problems differently

Most therapies encourage, directly and indirectly, new ways of confronting real-life problems. In some, such as behavioural treatments, changed action and experimentation is an integral part of treatment; in others, such as psychoanalysis, clients are reorientated psychologically to their own experience, and are expected to change their lives on their own. It has been hypothesised that even placebo treatments encourage mental or behavioural experimentation: the very belief that treatment has been administered leads clients to re-enter the problem situation and test the hypothesis that they have been cured (Bootzin & Lick, 1979).

Why have sham treatments not been invented to simulate these 'reorganising' non-specific factors? Perhaps because it is not possible. If the labelling process, or the conceptual schematising of problems, or of change, or the rethinking of context, are themselves therapeutic, then any sham version of them runs the risk of becoming a therapy in its own right. How can one invent credible placebo labelling, for instance? By using nonsense syllables? Some procedures, indeed, which were designed as sham controls, have been criticised for being active specific treatments (Garfield, 1983).

Therapeutic Impact

Therapeutic impact is the capacity of an intervention to overcome clients' tendencies to ignore it, neglect it, habituate to it, or forget it (Omer, 1987). Arousal, surprise, and investment of effort are three aspects of therapeutic interventions which give them impact.

Arousal helps to prevent lack of impact by inattention. Emotionally arousing therapies may be effective because they cannot be easily ignored rather than because of any specific value of the emotional events expressed in them. Even enhancing arousal artificially, such as by giving ether, has been shown to facilitate therapeutic change (Hoehn-Saric, 1978).

Surprising interventions may counter lowered impact produced by habituation effects (i.e. decreasing response to repetitive or expected stimuli) (Omer, 1987). Such effects might explain Silverman & Beech's (1984) finding that one-session interventions have a disproportionately strong impact and the fact that Smith *et al* (1980) found longer treatments no more effective than shorter ones. Therapies whose tactics surprise clients, as is common with new ones, may be more effective early in their careers precisely because clients have no habitual expectations about them.

Therapies which demand great effort may be more effective than others because clients will be less likely to forget them or trivialise them. Whether hypnotic treatments for stopping smoking use similar or different specific interventions, for instance, their effectiveness differs according to how much effort they require of clients (Omer, 1987). This may be true of other treatments too.

The levels of arousal, surprise, and effort induced by sham treatments have not been assessed. We expect that they are routinely lower than those induced by real treatments. In any case, the creation of convincing sham treatments which account for these variables, even if possible, might demand more skills and effort than real therapy does.

Conclusions

Research applications

Like Wilkins (1979, 1983), Parloff (1985), and Horvath (1987), we doubt that it is possible to design useful no-treatment or sham-treatment groups to control for non-specific effects. Fortunately, the relative efficacy of psychological treatments may be demonstrated well enough by comparisons between treatments, making placebo controls unnecessary (Parloff, 1985), or by comparisons with meta-analytic summaries (Critelli & Neumann, 1984). Such comparisons should also attend to the probable contribution of non-specific factors, but there is no good methodology for doing this at present. Diverse treatments may differ in quality of therapeutic relationship, expectancy, organising factors, and impact, and developing dependable procedures for assessing these non-specific factors when real treatment is given may be far more important than the chimerical pursuit of credible shams.

Placebo groups, as usually conceptualised, also have little to contribute to the study of therapeutic mechanisms, which demands the careful dismantling of potential therapeutic factors, and there is no place in it for a waste-basket category of non-specific noise.

Practical and theoretical implications

Psychotherapy is presently enjoying an ecumenical atmosphere in which dialogue between schools proliferates (London, 1984). Discussion of non-specific factors has contributed to this change by helping to overcome divisions (Omer & London, 1988) and to a common language across schools (Goldfried, 1980; Messer, 1986). Non-specific factors are also leading to new therapeutic theories linking treatment to cognitive and social psychological (Bandura, 1977; Strong & Claiborn, 1982) as well as to 'meta-techniques', which can be used with many specific approaches (Omer, 1986, 1987).

Professionalism and training

Training psychotherapists is a complex undertaking. One cannot learn to use non-specific factors except in the context of learning specific techniques. Far from implying that psychotherapy is merely "the purchase of friendship" (Schofield, 1964), our analysis suggests that therapists' technical expertise depends on how they manage the combination of non-specific with specific interventions. Apart from other techniques, all therapists must learn how best to steer the relationships, how to enhance positive and realistic expectancies, how to promote reorganisation of the client's perspective, and how to have maximum impact. Professional training should focus equally on specific techniques and non-specific skills.

References

BANDURA, A. (1977) Self-efficacy: toward a unifying theory of behavioral change. *Psychological Review*, **84**, 191–215.

BARTON, A. (1974) *Three Worlds of Therapy: An Existential-Phenomenological Analysis of the Therapies of Freud, Jung and Rogers* (pp. 185–246). Palo Alto: National Press.

BENNIS, W. G., BERLEW, D. E., SCHEIN, E. H. *et al* (eds) (1973) Personal change through interpersonal relationships. In *Interpersonal Dynamics: Essays and Readings on Human Interaction* (pp. 237–266). Homewood, Illinois: The Dorsey Press.

BOOTZIN, R. R. & LICK, J. R. (1979) Expectancies in therapy research: interpretive artifact or mediating mechanism? *Journal of Consulting and Clinical Psychology*, **47**, 852–855.

BORKOVEC, T. D. & NAU, S. D. (1972) Credibility of analogue therapy rationales. *Journal of Behavior Therapy and Experimental Psychiatry*, **3**, 257–260.

BRODY, N. (1983) Where are the emperor's clothes? *Behavioral and Brain Sciences*, **6**, 303–310.

COHEN, J. (1969) *Statistical Power Analysis for the Behavioral Sciences*. New York: Academic Press.

CORNSWEET, C. (1983) Nonspecific factors and theoretical choice. *Psychotherapy: Theory, Research and Practice*, **20**, 307–313.

CRITELLI, J. W. & NEUMANN, K. F. (1984) The placebo: conceptual analysis of a construct in transition. *American Psychologist*, **39**, 32–39.

FRANK, J. (1961) *Persuasion and Healing* (1st edn). Baltimore, MD: Johns Hopkins University Press.

—— (1973) *Persuasion and Healing* (revised edn). Baltimore, MD: Johns Hopkins University Press.

GARFIELD, S. L. (1983) Does psychotherapy work? Yes, no, maybe. *Behavioral and Brain Sciences*, **6**, 292.

GOLDFRIED, M. R. (1980) Toward the delineation of therapeutic change principles. *American Psychologist*, **35**, 991–999.

GOLDSTEIN, A. P. (1962) *Therapist-Patient Expectancies in Psychotherapy*. New York: Pergamon Press.

HAHN, R. A. (1985) A sociocultural model of illness and healing. In *Placebo: Theory, Research and Mechanisms* (eds L. White, B. Tursky & G. E. Schwartz (pp. 167–195). New York: Guilford Press.

HALEY, J. (1963) *Strategies of Psychotherapy*. New York: Grune and Stratton.

HARRIS, M. J. & ROSENTHAL, R. (1985) Mediation of interpersonal expectancy effects: thirty-one meta-analyses. *Psychological Bulletin*, **97**, 363–386.

HOEHN-SARIC, R. (1978) Emotional arousal, attitude change, and psychotherapy. In *Effective Ingredients of Successful Psychotherapy* (eds J. D. Frank *et al*). New York: Brunner/Mazel.

HORVATH, P. (1987) Demonstrating therapeutic validity versus the false placebo-therapy distinction. *Psychotherapy*, **24**, 47–51.

JUSSIM, L. (1986) Self-fulfilling prophecies: a theoretical and integrative review. *Psychological Review*, **93**, 429–445.

KARASU, T. B. (1986) The specificity versus nonspecificity dilemma: toward identifying therapeutic change agents. *American Journal of Psychiatry*, **143**, 687–695.

KIRSCH, I. (1978) The placebo effect and the cognitive-behavioral revolution. *Cognitive Therapy and Research*, **2**, 255–264.

—— (1985) Response expectancy as a determinant of experience and behavior. *American Psychologist*, **40**, 1189–1202.

LONDON, P. (1984) Ecumenism in psychotherapy. Review of Goldfried, M. R. (ed.) *Converging Themes in Psychotherapy*. *Contemporary Psychology*, **28**, 507–508.

MESSER, S. B. (1986) Eclecticism in psychotherapy: underlying assumptions, problems, and trade-offs. In *Handbook of Eclectic Psychotherapy* (ed. J. C. Norcross) (pp. 379–397). New York: Brunner/Mazel.

MURRAY, E. J. & JACOBSON, L. I. (1971) The nature of learning in traditional and behavioral psychotherapy. In *Handbook of Psychotherapy and Behavior Change: An Empirical Analysis* (eds A. E. Bergin & S. L. Garfield) (pp. 909–950). New York: John Wiley & Sons.

OMER, H. (1986) Integrating paradoxical interventions in the normal course of therapy. *American Journal of Psychotherapy*, **40**, 572–581.

—— (1987) Therapeutic impact: a major neglected factor in directive psychotherapy. *Psychotherapy*, **24**, 52–57.

—— & LONDON, P. (1988) Metamorphosis in psychotherapy: end of the systems era. *Psychotherapy*, **25**, 171–180.

PARLOFF, M. B. (1985) Placebo controls in psychotherapy research: a sine qua non or a placebo for research problems? *Journal of Consulting and Clinical Psychology*, **54**, 79–87.

—— (1986) Frank's "common elements" in psychotherapy: nonspecific factors and placebos. *American Journal of Orthopsychiatry*, **56**, 521–530.

PATTERSON, C. H. (1985) What is the placebo in psychotherapy? *Psychotherapy*, **22**, 163–169.

PENTONY, P. (1982) *Models of Influence in Psychotherapy*. New York: The Free Press.

PRIOLEAU, L., MURDOCK, M. & BRODY, N. (1983) An analysis of psychotherapy versus placebo studies. *Behavioral and Brain Sciences*, **6**, 275–310.

ROSENTHAL, D. & FRANK, J. D. (1956) Psychotherapy and the placebo effect. *Psychological Bulletin*, **53**, 294–302.

ROSENTHAL, R. (1974) *On the Social Psychology of the Self-fulfilling Prophecy: Further evidence for Pygmalion Effects and their Mediating Mechanisms*. New York: MSS Modular Publications.

SCHOFIELD, W. (1964) *Psychotherapy: The Purchase of Friendship*. Englewood Cliffs, NJ: Prentice Hall.

SHAPIRO, A. K. & MORRIS, L. A. (1978) Placebo effects in medical and psychological therapies. In *Handbook of Psychotherapy and Behavior Change: An Empirical Analysis* (2nd edn) (eds S. L. Garfield & A. E. Bergin), pp. 369–410. New York: John Wiley & Sons.

SHAPIRO, D. A. (1981) Comparative credibility of treatment rationales: three tests of expectancy theory. *British Journal of Clinical Psychology*, **21**, 111–122.

SHEPHERD, M. (1983) Psychotherapy outcome research and Parloff's pony. *Behavioral and Brain Sciences*, **6**, 301–302.

SILVERMAN, W. H. & BEECH, R. P. (1984) Length of intervention and client assessed outcome. *Journal of Clinical Psychology*, **40**, 475–480.

SMITH, M. L., GLASS, G. V. & MILLER, T. I. (1980) *The Benefits of Psychotherapy*. Baltimore, MD: Johns Hopkins University Press.

SPENCE, D. P. (1982) *Narrative Truth and Historical Truth: Meaning and Interpretation in Psychoanalysis*. New York: W. W. Norton.

STRONG, S. R. & CLAIBORN, C. D. (1982) *Change Through Interaction: Social Psychological Processes or Counselling and Psychotherapy*. New York: John Wiley & Sons.

UHLENHUTH, E. H., RICKELS, K., FISHER, S. *et al* (1966) Drug, doctor's verbal attitudes and clinical setting in the symptomatic response to pharmacotherapy. *Psychopharmacologica*, **9**, 392–418.

WALLACH, M. S. & STRUPP, H. H. (1960) Psychotherapists' clinical judgments and attitudes toward patients. *Journal of Consulting Psychology*, **24**, 316–323.

WILKINS, W. (1979) Getting specific about nonspecifics. *Cognitive Therapy and Research*, **3**, 319–329.

—— (1983) Failure of placebo groups to control for nonspecific events in therapy outcome research. *Psychotherapy: Theory, Research and Practice*, **20**, 31–37.

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Brief Reports

Epilepsy and Violence

C. G. HINDLER

Epileptic automatism and violence are seldom found among temporal lobe epileptics. The case of a 19-year-old girl who killed a 20-month-old child during an epileptic attack is described, and the literature and medico-legal issues are briefly reviewed.

Automatism can occur either as a direct result of a seizure discharge (i.e. an ictal event), or post-ictally. The amygdaloid–hippocampal structures are involved bilaterally, and therefore memory will be affected (Fenton, 1972). The resultant behaviour varies greatly from patient to patient, and in the same individual on different occasions (Knox, 1968). The motor actions have a well co-ordinated quasi-purposeful quality, but are often inappropriate, judgement is impaired, and sometimes the patient has a fixed, staring gaze (Fenton, 1972).

The following is a report of an unusual case of medico-legal interest, where violence occurred during an epileptic seizure.

Case report

Miss A, a nanny aged 19, was seen at the request of her solicitors. She was accused of murdering a 20-month-old baby who had been in her care.

Miss A described episodes of strange sensations resulting in her head feeling muzzy, a feeling of emptiness, and then a sensation as if her mind were separate from her body. She would then experience intense feelings of hate and aggression, which were always directed at the child. These episodes began a few weeks before the offence. She said that it was impossible to control her feelings or actions during these periods, although on occasion she was able to walk out of the room until the feeling subsided. She stated that they lasted perhaps five to ten minutes, but was unsure, as she felt a loss of sense of time.

It appears that the 'trigger' for each of these events involved the baby laughing, when she would feel irritable, develop a pain in the left temple, experience an odd smell, and then feel a difficulty in breathing, an intense excitement and hate, blurring of her peripheral vision, and a sense of acting like a puppet. The episodes were terminated by the baby's crying. Afterwards, she would at times have a headache, and often felt extremely upset and guilty.

There did not appear to be any loss of consciousness, but her description suggested an altered state of consciousness. The patient denied ever blacking out, any incontinence, or having a 'shaking fit'. She experienced these attacks only while alone with the baby. She remembered swinging the baby violently, and on one occasion she bit the child's leg. On the day of the offence, she had been swinging the child by the legs. The baby's head hit a cabinet and perhaps the floor. She called an ambulance, but the baby died eight days later. Post-mortem findings were of cerebral oedema consistent with child battering.

Miss A had a normal birth and normal milestones, with no neurotic symptoms in childhood. She did, however, suffer from febrile convulsions up to the age of seven. She attended a mixed comprehensive school and was successful academically. She gained a City and Guilds Examination in home economics and family care, and her ambition was a career in child care. This was her first job as a nanny.

She described herself as a loner when a child, but during her adolescence mixed well with her peers. She denied having boyfriends or sexual experience. Her menarche began at the age of 13, and there were no significant pre-menstrual symptoms. There was no history of illicit drug abuse or excessive alcohol intake, and no history of lying, stealing, fighting, truancy, or involvement with the police. She had never experienced any serious illness or head injury.

There was no family psychiatric history. She had a good relationship with her parents, and there was no suggestion of an abnormal family environment. Her younger sister, aged 17, suffers from focal epilepsy.

On mental state examination, Miss A presented as pleasant, co-operative, and passive. She was reported as being a conscientious, compliant person. Questioning revealed that she had experienced *déjà vu* and *jamais vu*, as well as abnormal olfactory odours and feelings of derealisation. There was no persistent disorder of thinking, perception, or affect. Cognitive testing revealed no abnormality.

While on remand in prison, she described three episodes of the abnormal experiences described above, and was witnessed hitting a cupboard and thumping her bedside cabinet, but had amnesia for her actions. On one of these occasions she was seen by her doctor to have a generalised epileptiform convulsion.

An EEG read by a consultant who had no knowledge of the case was recorded as follows: "the record contains numerous bursts of epileptogenic activity. The basic background activity consists of 10 Hz 20–50 μV symmetrical alpha rhythm which blocks on eye opening. This is often interrupted by generalised bursts of fairly symmetrical spike and wave activity although at times appearing with greater voltages in the frontal regions or with a left posterior prominence. Phase reversing posterior sharp–slow waves occur irregularly throughout the recording with a slight right-sided prominence. Hyperventilation enhances the right-sided posterior sharp–slow waves. Binocular photic stimulation elicits generalised paroxysmal responses at flash rates of approximately 12 flashes/second. Monocular stimulation blocks this paroxysmal activity." A full neurological investigation and computerised tomography revealed no abnormality.

Miss A pleaded guilty to manslaughter with diminished responsibility on the grounds of an abnormality of mind induced by disease within the terms of section 2 of the Homicide Act 1957. This plea was accepted by the court. After psychiatric evidence on behalf of the defence, she was put on probation with a condition of psychiatric in-patient treatment.

After hospital admission she had one further strange experience but without the aggressive feelings, during the early stages of treatment with carbamazepine. An EEG performed at this time showed only traces of paroxysmal abnormalities seen on the initial EEG. The generalised discharges had decreased but more discrete bitemporal/right temporal features persisted to a lesser extent.

Since then she has had no further abnormal experiences.

Discussion

The dilemma in this case was whether the symptoms suggesting temporal lobe epilepsy had been deliberately produced. The patient's sister suffers from epilepsy, and it would not be inconceivable for the patient to adopt the symptoms and rehearse the act of fitting. This would, however, suggest a certain amount of premeditation on her part, yet there appeared to be no motive for her to kill the child, and the act was completely out of character. Furthermore, the offence will obviously prevent her from working with children, which had been her ambition.

The occurrence of these episodes only in the presence of the baby is difficult to understand, but may be explained by a relatively rare phenomenon of 'reflex epilepsy'. This term is used for attacks which occur in response to some specific stimulus, for example 'musicogenic epilepsy' or 'television epilepsy' (Lishman, 1987). In her case, the precipitant was the baby's laughter.

Miss A would appear to have a genetic predisposition to epilepsy (her sister has epilepsy), and she had had febrile convulsions at an early age, which have been linked to mesial temporal lobe sclerosis on the basis of anoxia to this area of the brain. Mesial temporal lobe sclerosis is the commonest lesion found at temporal lobectomy, and occurs in some 50% of cases as the commonest single finding in epileptic patients who die a natural death (Lishman, 1987). Apart from childhood convulsions, there is, however, no history of proven epilepsy at a time independent of the criminal act, a criterion considered essential by Treiman (1986) when epilepsy is used as a defence.

Miss A described symptoms commonly occurring during an aura preceding a temporal lobe seizure. Auras lasting five to ten minutes are uncommonly long for complex partial seizures, but their content seems to have been similar for each episode, which is in keeping with such seizures. It is unusual for the content of the aura to be related to the act of automatism; in Miss A's case, the common theme centres on the child. It is, however, well known that behaviour during a complex partial seizure is to some extent determined by the circumstances in which the fit occurs (Fenton, 1972; Lishman, 1987). Distortion of sense of time is often an integral part of the experience of the aura, and hallucinations of smell derive from the medial temporal lobe structures, and are of great significance for the diagnosis of temporal lobe epilepsy. Strong affective experiences frequently appear, with fear and anxiety most common, but also anger, sometimes to an extreme degree. These affective disturbances are mainly associated with posterior temporal lesions, and the aroused affect is usually crude and stereotyped (Lishman, 1987).

The observation of Miss A experiencing seizures on three occasions, once by a doctor and twice by other prisoners, cannot be ignored. It is of interest, in terms of 'reflex seizures', that she was listening to music through headphones before and during one fit. She was also observed to engage in aggressive, semipurposeful disturbed motor behaviour, suggesting a psychomotor seizure. The act of swinging the child by the legs may be seen as a form of stereotyped motor behaviour or as organised directed aggression.

Psychomotor seizures are frequently preceded by aural manifestations. They may entirely displace the convulsion, and constitute the sole manifestation of the seizure. These forms of seizure have a special association with epilepsy originating in the medial temporal lobe structures. Epileptic automatisms are regarded as a subgroup of complex partial seizures. They are often preceded by aural manifestations, usually typical of temporal lobe epilepsy. The majority of patients with automatisms also suffer from other forms of seizures, especially grand mal attacks. Environmental cues may to some extent determine the detailed patterns of automatic behaviour. Lishman (1987) states that the essential and constant feature is amnesia for the period of automatism, which is usually total, although a vague and muddled awareness may be retained. Miss A did not have a dense amnesia for the events surrounding the offence, but certainly seemed to have had an altered level of consciousness, with some recall. The absence of amnesia is an important feature against the diagnosis of automatism. Considering the overall picture, however, it was felt that Miss A was suffering from temporal lobe epilepsy, and that the offence occurred during a state of automatism.

This case is noteworthy because of the rarity of violence in the course of ictal automatism (Gunn & Fenton, 1971; Gunn, 1978; Treiman, 1986; Lishman 1987). Secondly, the case is of interest because her defence was one of diminished responsibility under section 2 of the Homicide Act 1957, rather than a plea based on epileptic automatism.

Automatism and aggression

Automatisms are usually brief. Among Knox's (1968) 43 cases, 81% continued for five minutes or less, 12% between 5 and 15 minutes, and in no case did the automatism exceed one hour. Forty had experienced complete amnesia for the period of automatic behaviour, the remaining three having partial recall. No aggressive conduct was observed in 36 cases (84%). The remaining seven tended to resist any attempt to interfere with or restrict their activities, and only one of these patients was considered dangerous. Rodin (1973) found only one out of 150 patients to be aggressive. He also found that if a patient was restrained during the confusional state, he might react in a defensive manner that could be misinterpreted as a goal-directed assault. In the study by Delgado-Escueta *et al* (1981) 19 patients who were believed to be aggressive during seizures were selected from a group of approximately 5400 patients with epilepsy. Of these 19, only one committed aggressive acts that could have resulted in serious harm to another person. King & Ajmone Marsan (1977) studied 199 patients with various types of seizures, and reported nine instances that they could define as peri-ictal violence. Gunn & Bonn (1971) investigated criminality and violence among epileptic prisoners. Using a census of prison and borstal receptions performed in 1966, they found a prevalence of epilepsy in prisons of 7.1 per thousand men (normal population 4.2 per thousand), although a representative sample of epileptic prisoners was no more criminally violent than a matched control group of prisoners. In fact, like other prisoners, the vast majority were not violent. They found that temporal lobe epileptics had a higher previous conviction rate, but that they were not prone to be convicted of offences of violence. Treiman (1986) concludes that prison prevalence rates for epilepsy are similar to those found in a number of underprivileged, lower socio-economic communities, such as those from which most British and American prisoners originate.

Fenwick (1986) found that the high prevalence of epilepsy among adult prisoners cannot be explained by any relationship between the biological aspects of epilepsy and proclivity towards violent actions. He states that factors found in excess among epileptics are low socio-economic status, increased perinatal morbidity, brain damage, and infections. It is thus possible that it is brain damage which is the important factor producing aggressive behaviour among epileptics rather than epilepsy *per se*. Prins (1986) elaborates further and states that a factor assuming greater prominence is an association between poor impulse control and brain damage. He also remarks that epilepsy itself produces its own social and psychological problems, which may result in antisocial behaviour. Delgado-Escueta *et al* (1981) suggest that if the content of epileptic automatisms has a psychodynamic meaning, a violent social background can conceivably result in more violent automatisms.

Medico-legal aspects

Two sorts of automatism, insane and non-insane, are recognised by English courts as a consequence of the case of *R* v. *Kemp* in 1957 (see Walker, 1968). A verdict of non-insane automatism is based on a state which is not regarded as a disease of the mind (such as sleep walking or concussion) and results in an acquittal. By contrast the outcome of a verdict of insane automatism is admission to a hospital specified by the Secretary of State without limit of time (*British Medical Journal*, 1973, 1983). The case of *R* v. *Sullivan* in 1983 confirmed that in law, an act committed in a state of epileptic automatism is regarded as an insane automatism (see *British Medical Journal*, 1983). According to the judgement made in the case of *R* v. *Kemp*, the law makes no distinction between a disease of the mind that is derived from a functional illness and that derived from degeneration of the brain. It is also legally determined that the permanent or temporary nature of the disorder is unimportant, as is the potential for treatment. Hence the law appears more concerned with the state of mind of the defendant at the time of the alleged offence than with the notion of disease (Eastman, 1986).

In the case of Miss A, it appears that there was a possibility that she committed the act during the aura, rather than during the ictal or post-ictal period. She was not unconscious at the time of the act, and as she was suffering from a treatable condition it was desirable to plead diminished responsibility rather than automatism. In the light of the *Sullivan* verdict a plea based on epileptic automatism would have resulted in a verdict of not guilty by reason of insanity and compulsory hospital admission.

Conclusion

It is important to have some criteria in order to assess the probability of a crime having been committed during an episode of epileptic automatism. The following is an amalgamation from various authors (Fenton, 1972; Gunn, 1978; Lishman, 1987):

(a) a past history of unequivocal epileptic attacks
(b) the crime is out of character with the accused's previous personality
(c) the crime is motiveless and unpremeditated
(d) EEG studies are compatible
(e) an altered state of consciousness during the event
(f) total or partial amnesia for the crime.

The case of Miss A is in keeping with these criteria. From the medical point of view, informal admission as a condition of a probation order appeared to be a satisfactory outcome, as Miss A was fully co-operative and anxious to have treatment.

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References

British Medical Journal (1973) Defence of automatism (medico-legal news and notes). *British Medical Journal*, *ii*, 314–315.

—— (1983) Insanity at law (medico-legal report). *British Medical Journal*, **287**, 694–695.

Delgado-Escueta, A. V., Mattson, R. H., King, L., *et al* (1981) Special report: the nature of aggression during epileptic seizures. *New England Journal of Medicine*, **305**, 711–716.

Eastman, G. N. (1986) Psychiatric aspects of insanity and automatism. In *Psychiatry and the Criminal Process* (eds R. Mackay & K. Russell), pp. 15–25. Leicester: Polytechnic Law School Monograph.

Fenton, G. W. (1972) Epilepsy and automatism. *British Journal of Hospital Medicine*, January, 57–64.

Fenwick, P. (1986) Aggression and epilepsy. In *Aspects of Epilepsy and Psychiatry* (eds M. R. Trimble & T. G. Bolwig), pp. 31–60. Chichester: John Wiley and Sons.

Gunn, J. (1978) Epileptic homicide: a case report. *British Journal of Psychiatry*, **132**, 510–513.

—— & Bonn, J. (1971) Criminality and violence in epileptic prisoners. *British Journal of Psychiatry*, **118**, 337–343.

—— & Fenton, G. L. (1971) Epilepsy, automatisms and crime. *Lancet*, *i*, 1173–1176.

King, D. W. & Ajmone Marsan, C. (1977) Clinical features and ictal patterns in epileptic patients with EEG temporal lobe foci. *Annals of Neurology*, **2**, 138–147.

Knox, S. J. (1968) Epileptic automatism and violence. *Medicine, Science and the Law*, **8**, 96–104.

Lishman, W. A. (1987) *Organic Psychiatry*. Oxford: Blackwell Scientific Publications.

Prins, H. (1986) *Dangerous Behaviour, the Law and Mental Disorder*. London: Tavistock Publications.

Rodin, E. A. (1973) Psychomotor epilepsy and aggressive behaviour. *Archives of General Psychiatry*, **28**, 210–213.

Treiman, D. M. (1986) Epilepsy and violence: medical and legal issues. *Epilepsia*, **27** (suppl. 2), 77–104.

Walker, N. (1968) *Crime and Insanity in England*, vol. 1. *The Historical Perspective*. Edinburgh: Edinburgh University Press.

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Pimozide in Pathological Jealousy

ALAN BYRNE and LAKSHMI N. YATHAM

A 39-year-old man had his pathological jealousy successfully treated with pimozide. It is suggested that pimozide might be considered the drug of choice in all the monodelusional disorders.

Pathological jealousy can occur in relation to a number of conditions – chronic alcoholism, organic brain disorder, schizophrenia or affective disorder (Seaman, 1979) – or it may present as the only delusion in delusional disorder (DSM-III-R, American Psychiatric Association, 1987). The essential feature is a delusional belief that the marital partner is being unfaithful. Various forms of treatment have been tried, including phenothiazines (Mooney, 1965), behavioural therapy (Cobb & Marks, 1979), individual psychotherapy (Seaman, 1979) and family therapy (Modlin, 1963), all with limited success. We report the successful use of pimozide in the treatment of pathological jealousy, and examine the other monodelusional disorders which respond to pimozide.

Case report

Mr G, a 39-year-old man seen as an emergency in our unit following referral from his general practitioner, described 'slight' problems with his wife, as she had apparently left home for no reason a week earlier. He indicated that the relationship with his wife had deteriorated, and that if she were to leave him for good, he would commit suicide. He was admitted to the ward.

Mr G's wife revealed the true situation - she had left home because of his abnormal jealous behaviour. This had culminated in his bringing a knife to the local public house in order to protect himself from her supposed lovers. Mr G wept bitterly when questioned about his wife's history. He admitted to having 'crazy' feelings over the previous four years, imagining that his wife was being unfaithful with any man she met. He had accused her of having affairs with dozens of men, and questioned her at length about her clothes, especially her underwear. He believed she wore dramatic lingerie to excite her various lovers. Mr G, being unemployed, insisted on going everywhere with his wife, and even managed to join ladies groups to monitor her activities. The jealousy was always increased by alcohol consumption, and the incident in which he carried the knife for protection had followed moderate alcohol intake. Mrs G left the house because of threats of physical violence, which she had experienced before.

Previous psychiatric history was unhelpful, but family history revealed evidence of pathological jealousy in the patient's father. This had resulted in his forcible expulsion from the family home, and he subsequently died of alcohol-related problems at the age of 53. Of note in his previous medical history, Mr G had received treatment for a severe pernicious anaemia three years before the admission in question, and he was on maintenance vitamin B12 injections on admission. Mr G was commenced on pimozide (2 mg b.d.), and appeared to settle well. His jealous ideas became amusing to him as he gained insight into their bizarre nature and realised the unreasonableness of his accusations regarding his wife. In view of the alcohol component, he agreed to commence disulfiram to improve his chances of recovery.

Mr G was discharged from hospital after two weeks. He continues on pimozide (2 mg) and on disulfiram, and he is doing well. His wife has returned to the family home and confirms that there is now no evidence of pathological jealousy. Mr G tried alcohol once since discharge, and was deterred by nausea and flushing. He continues to do well on pimozide.

Discussion

This patient's presentation is typical of pathological jealousy, where there is often a serious threat to the life of the spouse. This case meets the DSM-III-R criteria for a diagnosis of delusional disorder, jealous subtype. It is unlikely that the pernicious anaemia was causally related, as the morbid jealousy antedated the anaemia and did not respond to replacement therapy.

DSM-III-R subtypes delusional disorders as somatic, jealous, erotomanic, grandiose, persecutory and non-specific. Monosymptomatic hypochondriacal delusional psychosis seems to fall into the somatic category, and it is now well established that pimozide, a diphenyl-butyl-piperidine, is very effective in the treatment of this form of disorder (Munro, 1982). Dorian (1979) was the first to report the successful treatment of pathological jealousy with pimozide. Since then, two other reports have been published (Pollock, 1982; Munro, 1984), and in both response to pimozide was felt to be excellent. Erotomania, another subtype of delusional disorder, has also been shown to respond to pimozide (Munro *et al*, 1985).

Kendler *et al* (1985) argued that delusional disorders are quite separate from schizophrenic disorders, based largely on family studies which usually show no excess of schizophrenia in the relatives of probands with delusional disorder. The absence of a family history of schizophrenia and the positive family history of pathological jealousy in our case tend to support this view. This area would benefit from further exploration in well designed studies.

We suggest that pimozide might be considered the drug of choice in pathological jealousy and all the monodelusional disorders.

References

American Psychiatric Association (1987) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn) (revised) (DSM-III-R). Washington, DC: APA.

Cobb, J. P. & Marks, I. M. (1979) Morbid jealousy presenting as obsessive-compulsive neurosis : treatment by behavioural psychotherapy. *British Journal of Psychiatry*, **134**, 301-305.

Dorian, B. J. (1979) Monosymptomatic hypochondrical psychosis. *Canadian Journal of Psychiatry*, **24**, 377.

Kendler, K. S., Masterson, C. C. & Davies, K. L. (1985) Psychiatric illness in first degree relatives of patients with paranoid psychosis, schizophrenia and medical illness. *British Journal of Psychiatry*, **147**, 524-531.

Modlin, H. (1963) Psychodynamics in management of paranoid states in women. *Archives of General Psychiatry*, **8**, 263.

Mooney, H. B. (1965) Pathological jealousy and psychochemotherapy. *British Journal of Psychiatry*, **111**, 1023-1041.

Munro, A. (1982) *Delusional Hypochondriasis. Clark Institute of Psychiatry Monograph*, series 5. Toronto: Clark Institute of Psychiatry.

—— (1984) Pathological jealousy, an excellent response to pimozide. *Canadian Medical Association Journal*, **131**, 852–853.

——, O'Brien, J. W. & Roll, D. (1985) Two cases of "pure" or "primary" erotomania successfully treated with pimozide. *Canadian Journal of Psychiatry*, **30**, 619–622.

Pollock, B. G. (1982) Successful treatment of pathological jealousy with pimozide. *Canadian Journal of Psychiatry*, **27**, 86–87.

Seaman, M. (1979) Pathological jealousy. *Psychiatry*, **42**, 351–361.

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A Chinese Classic Phenylketonuria Manifested as Autism

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A 12-year-old Chinese boy had a diagnosis of infantile autism at infancy that was finally confirmed as classic phenylketonuria at adolescence. This treatable inborn metabolic disease should be investigated in cases of apparent autism, especially where mass neonatal screening of inborn metabolic diseases has not been established.

Autism is a heterogeneous disease. The aetiology is still unknown, but biochemical dysfunction is likely to be of importance (Ritvo & Freeman, 1984). Classic phenylketonuria is an autosomal recessive disease, the victims suffering mainly from mental retardation (Tourian & Sidbury, 1983) which, if detected early enough, and treated properly, can be prevented (Colombo *et al*, 1980). Phenylketonuria manifesting as autism has been mentioned in the literature (Friedman, 1969), but has received little attention in the differential diagnosis of autism.

Phenylketonuria in Chinese has been reported in Taiwan (Hsiao *et al*, 1984) and mainland China (Liu & Zuo, 1986). The incidence in Chinese neonates, around 1/16 500, is similar to that in Caucasian children.

Case report

In April 1982, we carried out screening for congenital metabolic defects in mentally retarded children in Taiwan (Hsiao *et al*, 1984). A boy, attending a special private school for the handicapped, was found to have blood phenylalanine greater than 1200 μmol/l (normal $<$ 120 μmol/l) in primary screening by Guthrie's bacteria inhibition assay (Guthrie & Susi, 1963). Repetition of the screening test and further confirmatory tests by a fluorometric method (Tocci, 1982) supported the screening result of hyperphenylalaninaemia. Serum phenylalanine and tyrosine were 1815 μmol/l and 61 μmol/l, respectively. The urinary ferric chloride test was positive. Gas chromatography for the analysis of urinary organic acids (Hsaio *et al*, 1985) showed abnormally high concentrations of phenylpyruvic acid, phenylacetic acid, phenyllactic acid, and 2-hydroxyphenylacetic acid, which are abnormal metabolites of phenylalanine. Urinary pterins were determined by high-performance liquid chromatography (Niederwieser *et al*, 1982), and the ratio of biopterin to biopterin plus neopterin was 76% (reference range: 53.3–75.8%). Therefore atypical phenylketonuria caused by tetrahydrobiopterin deficiency was excluded. The boy was confirmed to have classic phenylketonuria.

In February 1983, when the diagnosis of phenylketonuria was confirmed, the boy was 12 years old, 145 cm tall, and 34 kg in weight, which is normal according to Chinese norms. His hair was brown, which is rare in normally black-haired Chinese. He had no physical handicaps. The boy was severely mentally retarded, flat in facial appearance with a distant attitude, isolated, and socially withdrawn. Occasionally he would laugh while on his own, and make strange utterances. He could not speak and would be periodically impulsively violent.

The boy has three older sisters, who are all of normal intelligence and mental state. The parents were not consanguineous. The sisters and parents gave negative results on tests for phenylketonuria.

The boy was delivered spontaneously at full term on 7 October 1970, without any complications. He was bottle fed. At first, he was regarded as normal because of his normal physical development, but the family came to feel there was something wrong about the child as he grew up. He did not develop language normally, and seemed poorly attached to the parents. He always sat alone, appeared self-centred, and showed no interest in his surroundings. He showed flattening of affect. In 1973, when three years old, he was sent to a public children's mental health centre in Taipei, and was diagnosed with infantile autism with severe mental retardation. He then started a special training programme in the centre. After one and a half years, his mental abilities did not improve, he was brought home, and cared for by his family.

In February 1978, at the age of seven, he became agitated, irritable, and was periodically impulsively violent. He was brought to the children's mental health centre again. An EEG showed no abnormalities, and according to the revised form of the Denver Developmental Screening Test (Frankenburg & Dodds, 1969), his developmental age was estimated at three years old. The patient was given oral methylphenidate (10 mg b.i.d.). One week later, his symptoms improved, and the drug was stopped.

In 1982, at the age of 11, he was again sent to a special private school for the treatment of his recurrent impulsive violent behaviour and unstable emotions. At that time he was diagnosed by the authors.

After confirmation of classic phenylketonuria, he received a low phenylalanine diet, and the serum phenylalanine was reduced from 1815 μmol/l to around 900 μmol/l, which was still higher than normal, but the boy became more emotionally stable. The frequency of impulsive behaviour decreased significantly, although his autistic behaviour did not improve. The diet therapy programme failed after six months, because it was very difficult for him to comply with it.

He reached puberty three years later, at the age of 15. His uncontrollable, impulsive, and violent behaviour became more disturbing. He was treated in our psychiatric clinic with chlorpromazine (50 mg t.i.d.), and his violent behaviour improved. His serum phenylalanine was 1200 μmol/l at this time. His family by this time were, however, reluctant to take care of him permanently, and he was sent to a long-stay mental institution.

Discussion

Phenylketonuria can cause many neurological and psychiatric symptoms (Friedman, 1969; Tourian & Sidbury, 1983). According to Lowe *et al* (1980), among 65 children with pervasive developmental disturbance (autism and atypical childhood psychosis), three were found to have phenylketonuria. In addition, an unrecognised adult phenylketonuric who was misdiagnosed with psychosis and received inappropriate treatment has been reported (Perry *et al*, 1973). In evaluating psychiatric disorders in adults and children, phenylketonuria and other congenital metabolic diseases should therefore be considered in the differential diagnosis, especially those disorders which may cause brain damage.

In Western European countries, America, and Japan, mass neonatal screening of congenital metabolic diseases has been carried out for years for the prevention of mental retardation (Bickel, 1980). In many developing countries, mass screening programmes have not yet been started, and the chances of encountering congenital metabolic diseases in psychiatric and neurological clinics seem much greater. This point should be kept in mind in order to prevent misdiagnosis.

Phenylalanine is the precursor of catecholamines. The biogenic amine theory is considered important in the exploration of the aetiology of psychiatric disorders. Abnormal biogenic amine metabolites have been found in autistic and atypical psychotic children (Gillberg & Svennerholm, 1987). There is also a report of autistic children who became schizophrenic when they grew up (Petty *et al*, 1984). The relationship between psychiatric symptoms and abnormally high concentrations of phenylalanine and its metabolites in phenylketonuria deserves further study.

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References

Bickel, H. (1980) Rationale of neonatal screening for inborn errors of metabolism. In *Neonatal Screening for Inborn Errors of Metabolism* (eds H. Bickel, R. Guthrie & G. Hammersen). New York: Springer-Verlag.

Colombo, J. P., Hammersen, G. & Bickel, H. (1980) Recommendations for newborn screening. In *Neonatal Screening for Inborn Errors of Metabolism* (eds H. Bickel, R. Guthrie & G. Hammersen). New York: Springer-Verlag.

Frankenburg, W. K. & Dodds, J. R. (1969) *Denver Developmental Screening Test*. Colorado: University of Colorado Medical Center.

Friedman, E. (1969) The autistic syndromes and phenylketonuria. *Schizophrenia*, 1, 249–261.

Gillberg, C. & Svennerholm, L. (1987) CSF monoamines in autistic syndromes and other pervasive developmental disorders of early childhood. *British Journal of Psychiatry*, **151**, 89–94.

Guthrie, R. & Susi, A. (1963) A simple phenylalanine method for detecting phenylketonuria in large populations of newborn infants. *Pediatrics*, **32**, 338–343.

Hsiao, K. J., Hung, S. H. Wu, S. J., *et al* (1985) Gas chromatographic analysis of abnormal urinary organic acids in phenylketonuria. *Journal of the Formosan Medical Association*, 84, 1240–1250.

Hsiao, K. J., Wuu, K. D., Sheen, F. M., *et al* (1984) Congenital metabolic diseases in mentally retarded Chinese children: screening for congenital hypothyroidism, phenylketonuria, galactosemia, maple syrup urine disease and homocystinuria. *Chinese Medical Journal*, 34, 31–32.

Liu, S. R. & Zuo, Q. H. (1986) Newborn screening for phenylketonuria in eleven districts. *Chinese Medical Journal*, 99, 113–118.

Lowe, T. L., Tanaka, K., Seashore, M. R., *et al* (1980) Detection of phenylketonuria in autistic and psychotic children. *Journal of the American Medical Association*, 243, 126–128.

Niederwieser, A., Matasovic, A., Staudenman, W., *et al* (1982) Screening for tetrahydrobiopterin deficiency. In *Biochemical and Clinical Aspects of Pteridines*, vol. 1 (eds H. Wachter, H. Ch. Curtius & W. Pfleiderer). Berlin: Walter de Gruyter.

Perry, T. L., Hansen, S., Tischler, B., *et al* (1973) Unrecognized adult phenylketonuria: implications for obstetrics and psychiatry. *New England Journal of Medicine*, 289, 395–398.

Petty, L. K., Ornitz, E. M., Michelman, J. D., *et al* (1984) Autistic children who become schizophrenic. *Archives of General Psychiatry*, 41, 129–135.

Ritvo, E. R. & Freeman, B. J. (1984) A medical model of autism: etiology, pathology and treatment. *Pediatrics Annals*, 13, 298–305.

Tocci, P. M. (1982) Phenylalanine, fluorometric method. In *Selected Methods of Clinical Chemistry* (eds W. R. Faulkner, S. Meites & S. V. Marcum). Washington, DC: American Association for Clinical Chemistry.

Tourian, A. & Sidbury, J. B. (1983) Phenylketonuria and hyperphenylalaninemia. In *The Metabolic Basis of Inherited Disease* (eds J. B. Stanbury *et al*). New York: McGraw-Hill Book Company.

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Depression-Dependent Exacerbation of Tardive Dyskinesia

PERMINDER S. SACHDEV

A middle-aged woman with a recurrent depressive illness showed worsening of her tardive dyskinesia during the depressive phases, with improvement on remission.

The relationship between tardive dyskinesia (TD) and the affective disorders is unclear. It has been suggested that patients with affective psychoses might constitute a high-risk group for the development of TD (Kane *et al*, 1980), but there is only anecdotal evidence for this. Chronic administration of antidepressants is reported to subsensitise the presynaptic dopamine receptors (autoreceptors), thereby increasing dopamine turnover (Chiodo & Antelman, 1980*a*), which should arguably decrease the risk of development of TD. Electroconvulsive therapy (ECT) has a similar influence on autoreceptors (Chiodo & Antelman, 1980*b*), but clinical reports have variously implicated it as a risk factor for TD (Curran, 1973) or suggested it as a treatment (Price & Levin, 1978). Any association between ECT and TD is unsupported by controlled evidence (Kane & Smith, 1982).

In the background of this uncertain relationship, this case report concerns a patient with DSM–III major depression, recurrent (American Psychiatric Association, 1980) and TD.

Case report

A 58-year-old woman with a 15-year history of more than 20 episodes of depression was admitted in a state of marked depression with melancholic features. She had been treated in the past with antidepressant and antipsychotic drugs, and four courses of ECT, and had been maintained on lithium for three years without significant impact on the frequency of her depressive episodes. She had received antipsychotic medication off and on over the years, equivalent to an average of 200–300 mg chlorpromazine per day over four years. Three years previously, she had been noted to have oral, lingual, and buccal dyskinesia suggestive of TD, as recorded in her chart, but this had not been quantified or adequately followed up.

When first admitted to our unit, she had marked withdrawal, psychomotor retardation, sleep disturbance, lack of appetite, pervasive lack of interest, and poverty of speech to the point of muteness. She had been off all medication for over three months before admission. Examination revealed continuous masticating movements of the jaw, choreo-athetoid movements of the tongue, and puckering of the lips typical of TD in the opinion of two psychiatrists and a neurologist. The jaw movements were so severe as to prevent her dentures from staying in place. Mild choreo-athetoid movements were present in the extremities.

She was treated initially with doxepin for one week, but because of marked psychomotor retardation ECT was instituted, with complete recovery after 12 treatments. All neuroleptics were avoided. Her involuntary movements decreased significantly as she improved, and were only mild in intensity when she was well. The movements were rated on the Abnormal Involuntary Movement Scale (AIMS; Guy, 1976) by the author on four occasions at weekly intervals during depression and remission. All ratings were done at 9 a.m. and not on the day of ECT. The mean AIMS sum 1–7 score for the depressed phase was 14.75 (range 14–16) and for the well phase 5 (range 4–6). There was no evidence of marked daily fluctuations in the intensity of the TD.

The patient was maintained on doxepin only (150 mg/day) after discharge from hospital. Mild TD continued. She had two further episodes of depression in the same year, with features similar to those already described. Both episodes were preceded by minor psychosocial stressors, and she had been compliant on her medication. These episodes were treated in hospital, for four and six weeks respectively, with an increase in the dose of the antidepressant. No further antipsychotic medication or ECT was instituted. During both these episodes, a similar worsening of her involuntary movements was recorded at the time of admission and on repeated assessment, with improvement on remission similar to that during the first admission (Fig. 1). The ratings during the well periods were significantly lower than those in the depressed phases ($P < 0.001$, one-tailed t-test). The AIMS ratings were again done by the author in the morning and at weekly intervals. A higher (250 mg/day) dose of doxepin was maintained on discharge after the third admission.

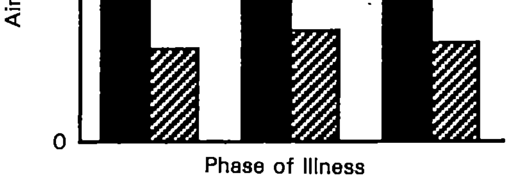

FIG. 1 Mean AIMS scores during three depressed (■) and well (▨) phases of the illness.

Discussion

This patient showed definite worsening of TD during phases of depression with improvement, though not complete remission, during normal intervals. It supports an earlier report of two patients by Cutler *et al* (1981) in whom dyskinesia consistently occurred during episodes of depression and disappeared during mania. The changes in our patient cannot be attributed to the treatment modality. She had been off antipsychotics for over three months before her first admission, and no antipsychotics were introduced subsequently. The TD was equally prominent while either ECT or antidepressant drug was used, and the patient was continued on the same dose of antidepressant during remission without worsening of the TD. The changes in intensity cannot be considered spontaneous fluctuations, as the range of scores was narrow in any one phase of the illness, random fluctuations in the dyskinesia were not observed clinically, and the intensity was fairly constant during remission throughout the period of observation. Further, the worsening during the depressive phase cannot be attributed to anxiety and agitation, as the illness was characterised by retardation and withdrawal. As the rater was not blind to the diagnosis, rater bias cannot be excluded, although the considerable difference in the ratings in different phases, the narrow range during one phase, and the fact that the ratings during the two initial phases were part of a standard assessment conducted routinely on in-patients with movement disorders argue against this.

The exacerbation of TD during an episode of depression is difficult to reconcile with the current understanding of the neurochemical disturbance in the two disorders. Post-synaptic supersensitivity of dopamine receptors is the generally accepted pathogenetic basis of TD (Marsden & Jenner, 1980). There is reportedly a temporary reduction in dopamine transmission associated with depression, especially depression characterised by psychomotor retardation (van Praag & Korf, 1971). This is suggested to cooperate with the pharmacological antagonism at dopamine receptors in provoking post-synaptic receptor supersensitivity, thereby increasing the long-term risk of TD in affective illness. However, if this reduced dopaminergic activity is accepted as a reliable finding (van Praag & Korf, 1971), there should be a state-dependent improvement of TD during depression. The observation in our patient was quite the opposite. The alternative neurochemical hypothesis of depression, postulating a role of hypersensitive post-synaptic monoamine receptors (Charney *et al*, 1981) in the pathogenesis, comes closer to explaining our finding. Most researchers, however, have paid little attention to dopamine in depression (van Praag, 1982); its role, if anything, is small. The role of the other monoaminergic systems have, likewise, received little attention in TD. This case report suggests that this situation should be redressed.

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References

American Psychiatric Association (1980) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn) (DSM-III). Washington, DC: APA.

Charney, D. S., Menkes, D. B. & Heninger, G. R. (1981) Receptor sensitivity and the mechanism of action of antidepressant treatment. *Archives of General Psychiatry*, **38**, 1160–1180.

Chiodo, L. A. & Antelman, S. A. (1980*a*) Repeated tricyclics induced a progressive dopamine autoreceptor subsensitivity independent of daily drug treatment. *Nature*, **287**, 451–454.

—— & —— (1980*b*) Electroconvulsive shock: progressive dopamine auto-receptor subsensitivity independent of repeated treatment. *Science*, **210**, 799–801.

Curran, J. P. (1973) Tardive dyskinesia: side effect or not? *American Journal of Psychiatry*, **130**, 406–410.

Cutler, N. R., Post, R. M., Rey, A. C., *et al* (1981) Depression-dependent dyskinesias in two cases of manic–depressive illness. *New England Journal of Medicine*, **304**, 1088–1089.

Guy, W. (1976) *ECDEU Assessment Manual for Psychopharmacology*. Washington, DC: US Department of Health, Education and Welfare.

Kane, J. & Smith, J. M. (1982) Tardive dyskinesia: prevalence and risk factors, 1959 to 1979. *Archives of General Psychiatry*, **39**, 473–481.

——, Struve, F. A., Weinhold, P., *et al* (1980) Strategy for the study of patients at high risk for tardive dyskinesia. *American Journal of Psychiatry*, **137**, 1265–1267.

Marsden, C. D. & Jenner, P. (1980) The pathophysiology of extrapyramidal side-effects of neuroleptic drugs. *Psychological Medicine*, **10**, 55–72.

Price, T. R. P. & Levin, R. (1978) The effects of electroconvulsive therapy on tardive dyskinesia. *American Journal of Psychiatry*, **135**, 991–993.

van Praag, H. M. (1982) Depression. *Lancet*, *ii*, 1259–1264.

—— & Korf, J. (1971) Retarded depression and the dopamine metabolism. *Psychopharmacology*, **19**, 199–203.

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A Case of Doll Phobia

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A case of doll phobia in a 14-year-old boy is presented and discussed.

A phobia is a special form of fear which is out of proportion to the demands of the situation, cannot be reasoned away, is beyond voluntary control, and leads to avoidance of the feared situation (Marks, 1969). The incidence of phobias in childhood, excluding school phobia, is thought to be low, although data are sparse. Marks (1969) quotes Graham, who reported ten specific phobias in 239 cases referred to a child psychiatric hospital, while Rutter *et al* (1970) found only 16 out of 2199 10- and 11-year-olds on the Isle of Wight with clinically significant and handicapping phobias. Graziano &

DeGiovanni (1979) report a total of 6.8% of children referred to behaviour therapists with fears that had lasted more than two years, or were of sufficient intensity to be debilitating.

The range of children's fears is legion; in Miller *et al*'s (1974) proposed nosology for childhood phobia, there are 78 different categories excluding school phobia. The same authors in their survey of 250 children between the ages of 7 and 13 asked about fears of masks, puppets, and furry toys, but none reported unreasonable or excessive fear of these objects.

The following case is unique, as it is the first time doll phobia has been described in the literature.

Case report

RP, a 14-year-old Hindu boy, was referred to the Child and Family Psychiatry Department at this hospital with life-long fear of dolls. The general practitioner's letter described him as "screaming with terror" in the presence of dolls. His parents had decided to seek help at this time because they had expected him to grow out of his fear as he got older, which had not happened.

RP was born in the UK, and his early development and education were normal. He attends a local private grammar school, and lives with his parents, who own an off-licence and general store. He has one 18-year-old sister. His family speak Gujarati, and RP is also fluent in English. There is no family history of psychiatric illness.

RP's first memory of being frightened by dolls was at the age of four, when he started attending nursery school. On occasions when he did see a doll, he felt panicky and if possible ran away. This was associated with a tachycardia and a feeling of pressure on the chest. He realised that he should not be afraid of dolls. The fear was worse with larger dolls, especially black ones, and was centred on the eyes and hair. If the eyes were mobile or the roots of the hair were visible on the doll's scalp, this increased the fear. His phobia, however, did not extend to other life-like toys, such as teddy bears or 'men' made out of building bricks. RP was more fearful of plastic dolls than rag ones. The more unusual the doll, the more scared he was. It did not make any difference to his phobic symptoms whether or not the doll was clothed or what sex it was. RP was not scared of pictures of dolls, but was mildly anxious when watching them on television.

His parents had tried to expose him to dolls at home, but this had resulted in RP panicking and running out of the room. Even so, RP on his own initiative had been able to approach and hold some small (10 cm high) Father Christmas figures which his parents had sold in their shop. He had not been able to extend this success to other dolls.

Because of his phobia his parents could not sell dolls in their shop, and neither his sister nor his female cousins could play with dolls near him, although they could play with other toys. RP would also avoid going into toy shops which might sell dolls, and would cross the road to avoid walking past shops which had dolls in their windows. He remembered that when he had been attending nursery school he had to avoid dolls, but otherwise his education had not been affected. In the past he had had nightmares about dolls, but these had ceased a few years previously.

There was no evidence that RP was morbidly anxious in other areas. On the Marks Fear Questionnaire (Marks, 1986) he scored within the normal range on the agoraphobic, blood, and social phobia subscales, yet he rated himself as "always avoiding dolls" and found his symptom "very severely disturbing/disabling". On the Hospital Anxiety and Depression Scale (Snaith & Zigmond, 1983) he scored zero on the depression subscale and four on the anxiety subscale, both of which are in the normal range. On mental state examination there was no evidence of depression or other psychiatric illness, apart from the presenting phobia. At the initial assessment interview he was tense and nervous, as he was expecting a doll to be introduced into the session. There was no evidence of any abnormal family relationships. RP related to his parents and sister in a mature, happy, consistent way, and he seemed genuinely distressed by his phobia.

Treatment consisted of a graded exposure to dolls *in vivo* over 12 weekly half-hour sessions, combined with exposure exercises given as homework between appointments. These would take the form of the author handling the doll, then getting RP to approach the doll and then hold it. He would hold the object until his anxiety began to lessen. He was then instructed to carry out the same exercise at home with the same doll for increasing amounts of time at least twice a day, and to keep a record of this. The record consisted of a self-assessment of anxiety using a nine-point scale with 0 being no anxiety and 8 panic, ratings being made before, during, and after exposure. RP also kept a record of how long he held the doll. The treatment began with a 10 cm rag doll, which he rated as 6 (marked anxiety) during exposure. Initially, he was unable to hold it. By the third session he was rating himself as 2 (slightly anxious) on exposure to the doll, and could hold it for longer than 15 minutes. The procedure was repeated with dolls of increasing size and realism, progressing in stages up to a 50 cm tall plastic black doll, with realistic hair and mobile eyes. Five different dolls were eventually used. It was agreed that he would move to the next stage when he had successfully overcome the fear aroused by the previous doll. At the end of this course of treatment RP was able to hold and look at large dolls with only slight anxiety. At follow-up ten months after presentation he was able to go into shops which sold dolls, and his cousins could play with dolls in his presence. On the Marks Fear Questionnaire he rated his phobic symptoms as only "slightly disturbing/not really disabling" and would only "slightly avoid" dolls. He also commented that he felt generally more confident in himself.

Discussion

Graziano *et al* (1979), in their extensive review of childhood fears, suggest that the intensity of a fear may be related to other behavioural pathology, such as temper tantrums. Rutter & Hersov (1985) also emphasise that it is rare to find a phobia as the only symptom in a child. In the case presented here the phobia was severe, but there was no evidence of any other psychopathology. What is surprising is that no cases of doll phobia have been reported previously, given the almost universal existence of dolls as children's toys in most cultures.

Acknowledgements

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References

GRAZIANO, A. M. & DEGIOVANNI, I. S. (1979) The clinical significance of childhood phobias: a note on the proportion of child-clinical referrals for the treatment of children's fears. *Behaviour Research and Therapy*, 17, 161–162.

——, —— & GARCIA, K. A. (1979) Behavioral treatment of children's fears: a review. *Psychological Bulletin*, 86, 804–830.

MARKS, I. M. (1969) *Fears and Phobias*. New York: Academic Press.

—— (1986) *Behavioural Psychotherapy: Maudsley Pocket Book of Clinical Management*. Bristol: Wright.

MILLER, L. C., BARRETT, C. L. & HAMPE, E. (1974) Phobias of childhood in a prescientific era. In *Child Personality and Psychopathology: Current Topics* (ed. A. Davids). New York: Wiley.

RUTTER, M. & HERSOV, L. (1985) *Child and Adolescent Psychiatry Modern Approaches*. Blackwell: Oxford.

——, TIZARD, J. & WHITMORE, K. (1970) *Education, Health and Behaviour*. New York: Wiley.

SNAITH, R. P. & ZIGMOND, A. S. (1983) The Hospital Anxiety and Depression Scale. *Acta Psychiatrica Scandinavica*, 67, 361–370.

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'Puerperal Psychosis' Following Male-to-Female Sex Reassignment?

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Psychosis is reported following abrupt withdrawal of oestrogen and surgery for male-to-female sex reassignment. The resemblance of the patient's mental state to puerperal psychosis suggested a hormonal aetiology.

Transsexualism is an unusual disorder of gender identity now given separate status by classification systems such as DSM–III (American Psychiatric Association, 1980) and ICD–10 (World Health Organization, 1987). Conservative estimates quote a prevalence rate for this disorder in England and Wales of 1 in 34 000 males and 1 in 108 000 females (Hoenig & Kenna, 1974), although the true prevalence may be greater. Persons with this condition frequently request surgery for sex reassignment, the indications for and against which pay considerable attention to the subject's personality and psychosocial functioning. In 1986, 195 operations for sex reassignment took place in the UK (45 National Health Service, 150 private sector) (Reid, personal communication) but more, approximately 1000 per annum, are performed in the United States.

Psychiatric complications following surgery for sex reassignment are reported in approximately 7% of cases, and are more common following male-to-female than female-to-male reassignment (Lothstein, 1982; Abramowitz, 1986). The literature also makes occasional reference to post-operative psychosis, and almost all instances of this have been after male-to-female reassignment. These psychotic disturbances are usually explained in terms of a catastrophic psychological reaction to a complex and extraordinary set of events. However, a further possibility which has not, so far, received comment in the literature is that these psychoses are related to the abrupt withdrawal of oestrogens that takes place at or shortly before surgery. Male-to-female transsexuals are usually prescribed feminising hormones for several years before being accepted for surgery. Some patients, in their haste to develop feminine bodily characteristics, also supplement their prescribed medication with hormones obtained from friends or other sources. Thus, the true dose may be considerable. An indirect reference to the possible role of oestrogen withdrawal in causing psychiatric complications in such patients was made by Wallinder & Thuwe (1975), who reported that long interruptions in hormone treatment were associated with unfavourable outcome.

The abrupt fall in oestrogen and progesterone after childbirth is widely accepted as having a role in causing puerperal psychoses in women. We report a phenomenologically similar case of psychosis in a man following male-to-female sex reassignment surgery, and which may be due to the same mechanism.

Case history

TL is a 34-year-old, unemployed, male-to-female transsexual who was admitted to a psychiatric unit in July 1987 five weeks after successful surgery for sex reassignment at another hospital. The first sign of mental disturbance was noted five days post-operatively, when the patient was described as "demanding and anxious". Diazepam was prescribed, and the patient was thought to have settled sufficiently at the time to be discharged home. Within a few days she became more disturbed and was demonstrating marked overactivity, disinhibited behaviour, sleep disturbance, and a variably irritable or elated affect. After admission, perplexity and confusion were noted to be prominent, but flight of ideas, pressure of speech, and grandiose non-delusional ideas, although present, were neither persistent nor prominent.

The patient's previous psychiatric history is unusually well documented as a consequence of participation in two unrelated research studies undertaken in 1975 and 1983. Salient features include long-standing gender identity disturbance, present from the age of four, and two previous episodes of minor depressive disorder (by Research Diagnostic Criteria) in 1976 and 1984. There is no previous history of hypomania and no family history of psychiatric disorder. On both occasions the patient described boyhood as happy, although the parental marriage was not stable; he truanted repeatedly from school, and learning difficulties necessitated placement at special schools. He ran away from home at the age of 14 after the break-up of his parents' marriage, and entered a predominantly promiscuous lifestyle, with periods of employment interspersed with prostitution. He never entered stable long-term employment, and began to live exclusively as a woman in 1975. He has no criminal convictions or history of substance abuse. However, his partner, with whom he had had an unstable relationship for seven years, does have a history of substance abuse and criminal conviction. Despite these factors, a number of opinions had been recorded (including that of his general practitioner) which testified to his dependent, affectionate, cheerful, and socially competent pre-morbid personality. His full-scale IQ in 1975 was assessed as 95.

Previous medical history includes secondary syphilis, which was diagnosed and adequately treated in 1985. From 1979 until the time of the operation he took feminising hormones (conjugated oestrogens: Premarin (5 mg t.d.s.) and Progynon (100 mg i.m.) monthly). It is not clear whether he supplemented this with black-market hormones. Although he denied doing so at the time of admission, he was known to associate with other transsexuals who were suspected of obtaining additional hormonal supplies.

Following formal admission to hospital on sections 2 and 3 of the Mental Health Act, the patient was prescribed neuroleptic medication (including haloperidol (20 mg t.d.s.)). The response to treatment was slow, partly because of continuing sensitivity to extrapyramidal side-effects. Nine weeks after admission, oral oestrogens were reinstated (Premarin (5 mg t.d.s.)) in order to obviate the osteoporosis which may develop following gonadal removal. It was noted that the patient's mental state improved considerably after this point, and two weeks later she was described as "relatively well" and able to go home for the weekend. She was finally discharged fit and well 15 weeks after admission and 22 weeks post-operatively. Her current medication was pimozide (4 mg daily) and Premarin (2.5 mg b.d.).

Relevant investigations during her stay showed a weakly (1/80) positive TPHA, but all other haematological, biochemical, and endocrinological investigations were normal. EEG and computerised tomography brain scan were also normal, but lumbar puncture, although attempted on two occasions, was unsuccessful. The patient declined further attempts to obtain cerebrospinal fluid and after further discussion with the neurologists this was abandoned. Neuropsychological testing performed shortly before discharge indicated some memory dysfunction, but this was inconclusive because of her reluctance to complete the assessment.

Discussion

There are several possible explanations for the mental changes seen in this patient. Even for those who long for sex reassignment, the surgery and post-operative adjustment to a new gender can be traumatic. A psychogenic model invoking object loss is an important consideration, but the duration and intensity of the patient's symptoms (five months) are uncharacteristic of purely psychogenic illness. A second possibility which cannot be excluded is that this disturbance represents the first manifestation of a bipolar affective disorder, although the two previous affective episodes were both of minor depression, and the family history was negative.

A first experience of mania following physical illness and drugs is described in the literature (e.g. Krauthammer & Klerman, 1978), and the relationship between the two is presumed to be direct, i.e. 'organic'.

Considerable discussion has taken place over the nosological status of puerperal psychoses, most examples of which resemble a hypomanic illness. However, certain features, typically perplexity, confusion, and labile affect, which are not usually apparent in hypomania, are often seen in puerperal psychosis, and are suggested as being distinctive of it (Brockington *et al*, 1982). Although the patient appeared to be suffering from a hypomanic illness, the authors were struck by the presence of these atypical features and the resemblance of her mental state to cases of puerperal psychosis. Further similarities between the two were also provided by the timing and sudden onset of the present disturbance, which occurred within a few days of the withdrawal of the oestrogens/surgery.

An extensive literature search for previous accounts of psychosis in relation to oestrogen withdrawal proved unsuccessful. Although there have been several attempts to link puerperal psychosis with progesterone, only one study was identified in which the role of oestrogen withdrawal was pursued (Hamilton, 1982). Hamilton gave oestrogen prophylaxis to 40 pregnant women who had experienced previous puerperal psychoses. Although these women stood a one in four/five risk of developing a further puerperal psychosis, not a single one of them did so. We suggest that an oestrogen withdrawal model might constitute a fruitful line of inquiry for future studies of 'puerperal psychosis'.

References

Abramowitz, S. I. (1986) Psychosocial outcomes of sex-reassignment surgery. *Journal of Consulting and Clinical Psychology*, **54**, 183–189.

American Psychiatric Association (1980) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn) (DSM–III). Washington, DC: APA.

Brockington, I.F., Winokur, G. & Dean, C. (1982) Puerperal psychoses. In *Motherhood and Mental Illness* (eds I. F. Brockington & R. Kumar), pp. 37–69. London: Academic Press.

Hamilton, J. A. (1982) The identity of post-partum psychosis. In *Motherhood and Mental Illness* (eds I. F. Brockington & R. Kumar), pp. 8–9. London: Academic Press.

Hoenig, J. & Kenna, J. C. (1974) The prevalence of transsexualism in England and Wales. *British Journal of Psychiatry*, **124**, 181–190.

Krauthammer, C. & Klerman, G. L. (1978) Secondary mania: manic syndromes associated with antecedent physical illness or drugs. *Archives of General Psychiatry*, **35**, 1333–1339.

Lothstein, L. M. (1982) Sex reassignment surgery: historical, bioethical, and theoretical issues. *American Journal of Psychiatry*, **139**, 417–426.

Wallinder, J. & Thuwe, I. (1975) *A Social-Psychiatric Follow-up Study of 24 Sex-Reassigned Transsexuals*. Goteborg, Akademiforlaget: Scandinavian University Books.

World Health Organization (1987) *International Classification of Diseases* (10th edn) (ICD–10), *1986 Draft of Chapter V*. Geneva: WHO.

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Syphilis Serology Screening in a Psychogeriatric Population

Is the effort worthwhile?

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The treponemal serological status of 800 patients above the age of 65 was reviewed. Twenty-one were found to be positive and the venereologists advised against treatment in all referred cases. The question is posed whether syphilis serology screening in the elderly mentally ill should be confined to those patients with obvious clinical manifestation of syphilis or with obscure psychiatric presentations.

Syphilis can present with a variety of mental symptoms from neurosis to psychosis and dementia. Lishman (1978) referred to it as "the most important infection of the nervous system encountered in psychiatric practice" and advocated that "serological tests for syphilis should be carried out in all patients admitted to psychiatric units". Response to adequate treatment is good, provided any recurrent activity is detected by serial examination of the blood and cerebrospinal fluid (CSF) and further treatment given.

TABLE I

Sex	*Age: years*	*Serology*				*Diagnosis*	*Treatment*
		VDRL	*TPHA*	*FTA*	*TPI*		
M	78	+	+	+	+	Depressive illness	No further action
F	72	+	+	+	+	Depressive illness	No further action
F	88	+	+	+	+	Late onset mania? Tertiary syphilis? Paraphrenic illness?	No further action
F	82	+	+	+	+	Senile dementia Depressive illness	No further action
F	85	+	+	+	+	Senile dementia Reactive depression	No further action
M	87	+	+	+	–	Senile dementia	No further action
F	80	+	+	+	?	Organic brain syndrome with symptomatic mania B12 deficient encephalopathy	No further action
F	85	+			+	Senile dementia	Treated by psychiatrist with benzyl penicillin for ten days
F	65	–	RPCFT positive			Reactive depression Organic brain syndrome	No action
F	85	+				Senile dementia Dysphoric mood	No action
F	82		WR positive			Senile and multi-infarct dementia	No action
M	74	+	+	+	+	Reactive depression	None
F	80	+	+	+	+	Senile dementia	None
F	87	+	+	+	–	Depression Mild cognitive impairment	None
F	75	+	+			Depressive illness	None
F	91	+	+			Paranoid schizophrenia Depressive illness? Recurrent acute organic brain syndrome	None
F	66	+	–	–	–	Senile dementia, Alzheimer's type	None
F	75	+				Neurotic depression Probable active syphilis (treated 40 years earlier)	None
F	72	+				Paranoid psychosis Subacute delirium	None
F	79	+	RPCFT positive			Senile dementia	None
F	92		WR positive			Depression Syphilis	None

VDRL, Venereal Disease Research Laboratory; TPHA, *Treponema pallidum* haemagglutination assay; FTA, fluorescent treponemal antibody; TPI, *Treponema pallidum* immobilisation assay; RPCFT, Reiter protein complement fixation test; WR, Wasserman reaction.

It is, however, clear that even in adequately treated patients, positive serology may persist for years and in some cases indefinitely (Davis *et al*, 1973; Schofield, 1979). The question arises, therefore, as to whether patients admitted to a psychogeriatric assessment unit should routinely have their treponemal serology status investigated. Will this reveal active cases who will benefit from treatment or will the high false positive rate of 20–40% and the likelihood of an adequately treated infection decades earlier make such screening futile?

There are few reports (Joffe *et al*, 1968; Dewhurst, 1969; Shannon *et al*, 1980) of elderly patients with neurosyphilis being treated, and little reference is made to outcome in this group (Giles, 1980). In this report the treponemal serology status of 800 patients assessed at a psychogeriatric assessment unit is reviewed, and the findings discussed.

Method

The assessment summaries of patients subjected to careful psychiatric and medical investigation during 1974–86 were reviewed. All patients with positive treponemal serology were identified. Data were gathered regarding the age, sex, psychiatric diagnosis, serological tests done, whether a venereologist was consulted, and treatment given.

Results

The results are shown in Table I. Of the 800 patients who were screened, 21 (2.6%) had positive treponemal serology (18 women, 3 men). Eleven of these patients (first 11 patients listed) were referred to a venereologist for advice and treatment, of whom seven had tests which were indicative of either untreated or latent syphilis (Dewhurst, 1969). Of the 11 patients referred, only one was treated, at the discretion of the psychiatrist, despite the venereologist's advice against this. Four of the ten non-referred patients fell into the category of untreated/latent syphilis. Nine of the patients referred to the venereologists had a diagnosis of an organic brain syndrome, while four of the non-referred patients had such a diagnosis. Further, in only three patients was syphilis considered to be an aetiological agent in the psychiatric disorder.

Discussion

Of all the patients screened for syphilis, 2.6% gave positive results. None were treated on specialist advice. Is there any point in doing the investigations? Luxon *et al* (1979) emphasised the need for such routine investigations in psychiatric practice, while Klein & Smith (1982) highlighted the fact that elderly persons may contract venereal disease. More importantly, however, they stress that syphilis may be latent for over 30 years before manifestations emerge. Banks (1968) and Bell (1959) have, however, questioned the activity of the spirochaete in patients over the age of 65. Indeed, none of their cases had any clinical evidence of active syphilis nor of any previous syphilitic process.

Unlike younger patients, in whom treatment is often instituted in the light of positive specific serological findings, despite the absence of clinical phenomena (Banks, 1968), the practice appears to be different in an elderly mentally ill population, as confirmed in the present study.

Schofield (1979) recommends that clinical and serological examinations should continue for life in cases of neurosyphilis, emphasising in particular the need for examinations of the cerebrospinal fluid (CSF). None of these patients had CSF investigations; should they have? There are very few cases reported where treatment has been instituted in an elderly mentally ill person (Joffe *et al*, 1968; Dewhurst, 1969; Luxon *et al*, 1979; Giles, 1980). The outcome of treatment has shown at best marked clinical improvement but with persistence of psychiatric phenomena (Giles, 1980), or minimal improvement with no further deterioration (Dewhurst, 1969). To date no follow-up studies of serologically positive elderly mentally ill patients who have received an adequate course of antisyphilitic treatment have been reported.

From the present findings the question arises as to whether syphilis serology in the elderly mentally ill patient should be confined to those with obvious clinical manifestations of syphilis or with obscure psychiatric presentations. Are the venereologists correct in advising psychogeriatricians to ignore positive serology in their patients? Is there any case for routine antisyphilitic treatment in all cases with positive serology in the hope that it may be beneficial? If no action is to be taken, should routine screening of this population be abandoned with consequent saving of money? Long-term follow-up of previously treated patients with positive serology to determine the incidence of subsequent psychiatric disorder, as well as a treatment study of those presenting with positive serology in old age, would help to provide some answers to these questions.

References

BANKS, G. D. (1968) The value of routine serological testing for syphilis in a mental hospital. *British Journal of Psychiatry*, **114**, 113–114.

BELL, R. E. (1959) The value of routine serological tests for syphilis on hospital admission. *American Journal of Clinical Pathology*, **32**, 521–525.

DAVIS, B. D., DULBECCO, R., EISEN, H. N., *et al* (1973) *Microbiology* (2nd edn). New York: Harper and Row.

Dewhurst, K. (1969) The neurosyphilitic psychoses today: a survey of 91 cases. *British Journal of Psychiatry*, **115**, 31–38.

Giles, A. J. H. (1980) Tabes dorsalis progressing to general paresis after 20 years despite routine penicillin therapy. *British Journal of Venereal Diseases*, **56**, 368–371.

Joffe, R., Black, M. & Floyd, M. (1968) Changing clinical picture of neurosyphilis: report of seven unusual cases. *British Medical Journal*, *i*, 211–212.

Klein, L. E. & Smith, C. R. (1982) Defusing a geriatric menace–latent V.D. *Geriatrics*, **37**, 125–132.

Lishman, W. A. (1978) *Organic Psychiatry*. Oxford: Blackwell.

Luxon, L., Lees, A. J. & Greenwood, R. J. (1979) Neurosyphilis today. *Lancet*, *i*, 90–93.

Schofield, C. B. S. (1979) *Sexually Transmitted Diseases* (3rd edn). Edinburgh: Churchill Livingstone.

Shannon, R., Copley, C. G. & Morrison, G. D. (1980) Immunological responses in late syphilis. *British Journal of Venereal Diseases*, **56**, 372–376.

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Contents: Use of seclusion in Scotland/Attitudes to seclusion in Virginia/Australian depression/Obstetric liaison/Practical administration of ECT/Haslam's schizophrenics/Compulsive water drinkers/Risk factors in schizophrenia/Antidepressant toxicity/Attitudes to anxiety/The epileptic arsonist/Treatment of extrapyramidal side-effects/Spontaneous orgasms – any explanations?

Use of seclusion in Scotland

SIR: Angold (*Journal,* April 1989, **154,** 437–444) provides a very useful review of the present state of knowledge about seclusion, and rightly emphasises the need for further research into its use. It is perhaps worth reporting that during 1985 the Mental Welfare Commission for Scotland undertook a review of the use of seclusion in psychiatric practice in Scotland, and for the purposes of its enquiry defined seclusion as: "removing a patient during daylight hours from the company of his fellow patients and staff and placing him, against his will, alone, in some form of constraining environment from which he cannot, of his own wish, remove himself".

The findings, described in the Commission's Annual Report, showed that in seven NHS psychiatric hospitals, containing some 4500 beds, seclusion was permitted, while in 14 psychiatric hospitals, containing some 9200 beds, seclusion was not permitted. The Commission made a variety of recommendations regarding the use of seclusion policies by Health Boards and the recording and reporting of incidents of seclusion.

In the following years it became apparent that hospitals were changing their policies and their use of seclusion, to the extent that when a further review was carried out in 1988, four of the hospitals previously using seclusion were no longer doing so, one hospital had seen only one episode of seclusion during the 3 years, and in only two hospitals was seclusion still made use of in any regular way. More recently still, Commissioners have met clinicians and Health Board representatives from these two hospitals, and it seems that a stage has been reached where in one of these hospitals seclusion is no longer being used, and in the other the practice of seclusion is being carefully re-examined.

Following its initial enquiry, the Commission found it hard to understand why seclusion should be used frequently in some psychiatric hospitals while in others, dealing with similar clinical problems, seclusion should have fallen into total disuse. The virtual disappearance of seclusion from all Scottish mental illness hospitals, with the exception of the State Hospital, makes it evident that this procedure is no longer a necessary part of the care of patients in ordinary psychiatric hospitals.

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Attitudes to seclusion in Virginia

SIR: Angold (*Journal,* April 1989, **154,** 437–444) states that it appears that the majority of patients dislike being locked up on their own. In a recent study (Wise *et al,* 1988) 111 current psychiatric patients were queried about their attitudes towards the use of seclusion rooms; 70% stated that it was a safe and secure room. Only 19% indicated that such rooms are torture, while the majority agreed that such rooms are helpful to patients in them. It is of interest that patients without a history of seclusion indicated stronger adverse feelings. In a follow-up study of 191 subjects (Wise *et al,* 1989), comparing patients on a unit with sequestered seclusion rooms with those on a unit with integrated seclusion rooms, patients in the latter group were more likely to agree that patients are often cured in such rooms. Both studies concluded that patients generally had positive attitudes about the utilisation of such treatment, and endorsed fairly realistic attitudes towards the experience.

It would be useful to discuss the role of seclusion with all patients during their orientation to the unit; this should reduce the distortions and fears of patients who will not utilise such facilities and also of those who may wish to utilise them.

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References

WISE, T., MANN, L., MURRAY, C. *et al* (1988) Attitudes of non-secluded patients toward seclusion rooms. *General Hospital Psychiatry*, **10**, 280–284.

——, ——, LEIBENLUFT, E., *et al* (1989) Isolated versus visible seclusion rooms: attitudes of psychiatric patients. *Psychiatric Quarterly* (in press).

Australian depression

SIR: It does seem better to be treated for depression in Australia (Lee & Murray, *Journal*, July 1989, **155**, 123–124). In our cohort there were 22 patients who presented with depression but in whom the final diagnosis made on the index episode was either schizophrenia, schizoaffective disorder, or organic psychosis. They were not included in any further follow-up studies. It is fortunate that we made the correct diagnosis at the beginning of the study.

We agree that we misinterpreted the first paragraph on p. 746 of Lee & Murray (1988). To be strictly comparable, we should have excluded our nine unnatural deaths from the bottom line of the first part of our Table IV. When we do so, the pattern of clinical criteria outcome for the remaining Sydney patients is more favourable, but the comparison with the Maudsley patients ($\chi^2=2.35$, d.f. $=2$, NS) remains non-significant. The second part of the table remains unaltered, and on the Lee–Murray criteria the Sydney patients did do better. Thus the conclusions drawn from Table IV (Kiloh *et al*, 1988) remain unchanged: being admitted to hospital in 1970 for depressive illness was, even in Australia, an event of serious import.

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References

KILOH, L. G., ANDREWS, G. & NEILSON, M. D. (1988) The long-term outcome of depression. *British Journal of Psychiatry*, **153**, 752–757.

LEE, A. S. & MURRAY, R. M. (1988) The long-term outcome of Maudsley depressives. *British Journal of Psychiatry*, **153**, 741–751.

Obstetric liaison

SIR: We were most impressed with the description given by Appleby *et al* (*Journal*, April 1989, **154**, 510–515) of the establishment of an obstetric liaison clinic. However, while appreciating that the main focus of their work was the identification of those women at risk for post-natal depression, we were nevertheless disappointed that they did not take a broader view in their discussion of further directions for the service, particularly in relation to substance misuse.

The catchment area served by their unit has a high prevalence of illicit drug users. Following the development of a Community Drug Team (CDT), we have witnessed an increase in the number of women presenting for treatment, with 38% of our total patient population being women, one-third of whom were caring for one or more children. This contrasts with a quarter of our patient population being women in previously published reports from our unit, and with the national figures from the Home Office Addicts Index (1989), in which 29% of new addicts in 1988 were female.

In the past two years, we have seen 20 pregnant women addicted to opiates in a cohort of 372 addicts who have been resident in the CDT catchment area (population 213 000). This indicates an annual incidence rate for pregnant opiate addicts of at least 4.0 per 100 000 catchment population, or 3.0 per 1000 births.

During this same period, we have witnessed the rapid spread of HIV through the drug-using population. The advent of HIV has increased the necessity to draw this high-risk population into contact with services. The ante-natal clinic, labour ward, and post-natal ward are areas where drug users are already being seen, although often without identification (or with late identification) of their drug problems. Staff in these services should make more of the opportunities for earlier identification and intervention.

There is now a pressing need for closer links between drug services and obstetrics services in an effort to limit the vertical spread of HIV and to provide appropriate support and help. The psychiatrist in the obstetric unit will be a vital link in this approach by encouraging the recognition and shared care of such patients.

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Sir: At Oslo City Hospital (Ullevål Sykehus) we are in the process of establishing a liaison psychiatric service to the obstetric unit. The service is provided by the child psychiatry liaison team rather than the adult psychiatrists, who instead respond to specific referrals from the child psychiatric team.

The prime aim is to facilitate parent-child adaptation to each other. This is based on a recognition that factors in both mother and child, and in the marriage, affect early interactions – and especially that the several factors play upon each other. With this primarily 'preventive' orientation, consultation has another angle to it that is missing when referrals are primarily of the mothers, as to an adult-orientated service. There is a reduced expectation of antenatal referrals, although these have been discussed with us.

The time is ripe to establish discussion between adult and child psychiatrists and their obstetrician colleagues about the directions for further developments in this field.

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Practical administration of ECT

Sir: The recent publication by the ECT Sub-Committee of the Research Committee (Freeman *et al*, 1989) is a welcome step towards unifying the practice of this useful, if ill-understood, treatment. I was especially pleased to see recognition of the nursing responsibilities involved (Appendix 15).

I am, however, surprised to find the recommendation that simple observation is probably sufficient for the routine monitoring of fit length. Christensen & Koldbæk (1982) found no predictable relationship between EEG manifestations and the observed seizure duration (OSD), and bifrontal single channel EEG tracings are fraught with interpretive difficulties (Brumback, 1983). However, when the comparatively simple cuff technique was used during administration of ECT then OSD did correlate with EEG activity, although with shorter recorded seizure times (Fink & Johnson, 1982).

At this centre, OSD is routinely recorded using the cuff technique to assist with the evaluation of individual treatment progress. There is a need for formal recording within ECT departments to facilitate both within-unit and between-unit review. A brief study of inter-rater reliability of OSD is being conducted here, with a view to establishing the usefulness of its contribution in this area.

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References

Brumback, R. A. (1983) EEG monitoring of ECT. *British Journal of Psychiatry*, **142**, 104–105.

Christensen, P. & Koldbæk, I. B. (1982) EEG monitored ECT. *British Journal of Psychiatry*, **141**, 19–23.

Fink, M. & Johnson, L. (1982) Monitoring the duration of electroconvulsive therapy seizures. *Archives of General Psychiatry*, **39**, 1189–1191.

Freeman, C., Crammer, J. L., Deakin, J. F. W., *et al* (1989). *The Practical Administration of Electroconvulsive Therapy (ECT)*. London: Gaskell.

Haslam's schizophrenics

Sir: I applaud Persaud & Allderidge (*Journal*, May 1989, **154**, 719–720) for drawing Dr Hare's attention to John Haslam's published descriptions of schizophrenics. I would, however, dispute their assertion that the writings of Haslam suggest that schizophrenic symptoms were nothing new, or so common that they were hardly worth mentioning. In fact, in a series of 29 Bethlem case histories (Haslam, 1798), only one is described as experiencing auditory hallucinations. Haslam did devote a whole book to the study of a patient, James Tilly Matthews, with clear symptoms of schizophrenic thought disorder (Haslam, 1810), but the very title of the book, which begins *Illustrations of Madness: Exhibiting a Singular Case of Insanity* ... does not suggest that the patient's symptoms were common, obvious, or hardly worth mentioning at all. Indeed, Thomas Monro, Haslam's immediate superior as Physician to Bethlem, was in no doubt as to the unusual and florid nature of Matthews' symptoms: "having scarcely in the whole period of his professional practice and experience known any patient more completely and equivocally mad" (Monro, 1809). Haslam's clinical descriptions of his patients are noted for their clarity and keenness of detail, and he would not have failed to record the symptoms of schizophrenia if he encountered them.

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References

HASLAM, J. (1798) *Observations on Insanity, with Practical Remarks on the Disease, and an account of the Morbid Appearances on Dissection*. London: F. and C. Rivington.

—— (1810) *Illustrations of Madness: Exhibiting a Singular Case of Insanity, and a No Less Remarkable Difference in Medical Opinions; Developing the Nature of Assailment, and the Manner of Working Events; with a Description of the Tortures Experienced by Bomb-Bursting, Lobster-Cracking, and Lengthening the Brain*. London: G. Hayden.

MONRO, T. (1809). *Deposition of Dr Thomas Monro*. Bethlem Archives, Box 60(8).

Compulsive water drinkers

SIR: Lee *et al* (*Journal*, April 1989, **154**, 556–558) describe the case of a 16-year-old Chinese girl with water intoxication following the ingestion of large quantities of water for traditional medicinal purposes. I was surprised to read the suggestion that the use of water to induce an altered state of consciousness (ASC) had not previously been described. Many of the patients I have seen with excess fluid intake present as 'drunk'; intoxication is defined in most dictionaries as including a feeling of excitement, exhilaration, and inebriation. Perhaps the usual description of the symptoms of water intoxication does not include pleasure as this is not something the patient complains about. The literature does contain references to ASC, though this title is not used. For example, Singh *et al* (1985) describe how Case 1, on becoming unemployed and thus no longer able to afford alcohol, turned to regular excessive water drinking because it "made him feel slightly drunk" (this paper is quoted by Dr Lee *et al*). In a more recent paper on the possible association between water intoxication and alcohol abuse, Ripley *et al* (1989) write that "mild overhydration may be experienced as pleasurable, leading to further polydipsia".

With regard to the case described, the authors make no mention of the girl's tobacco smoking habits, although they acknowledge that the clinical picture suggests a degree of SIADH (syndrome of inappropriate antidiuretic hormone secretion). Nicotine stimulates the release of arginine vasopressin, and thus may be significant in the aetiology of water intoxication and SIADH. Other associated factors in SIADH (according to Singh *et al*) are stress, head injury, medications (antipsychotics, anticonvulsants, diuretics, and anti-cancer drugs), and various medical conditions (especially malignancies).

If, as the authors imply, drinking large quantities of water is a culturally accepted practice in traditional Chinese medicine, I wonder if this girl's complications are unusual, and if so, why she specifically was so adversely affected.

The seeking of an ASC may be an aetiological link in a proportion of compulsive drinkers. It is not, however, a 'missing' link.

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References

RIPLEY, T. L., MILLSON, R. C. & KOCZAPSKI, A. B. (1989) Self-induced water intoxication and alcohol abuse. *American Journal of Psychiatry*, **146**, 102–103.

SINGH, S., PADI, M. H. & BULLARD, H. *et al* (1985) Water intoxication in psychiatric patients. *British Journal of Psychiatry*, **146**, 127–131.

Risk factors in schizophrenia

SIR: In their elegant study Baron & Gruen (*Journal*, April 1988, **152**, 460–465) found a greater familial risk for schizophrenia and schizophrenic spectrum disorders among probands born in the winter and spring than among those born during the remainder of the year. This finding is not in line with the major part of the pre-existing literature (Torrey, 1987), which primarily indicates an opposite trend. Aside from the results, the study also differs from previous ones in that it also considers the specific morbidity risk in first-degree relatives. In light of these discrepancies, we undertook a study to confirm whether schizophrenics born between December and April differ from those born during the other months of the year, both in relation to incidence of a family history of schizophrenia and to a familial morbidity risk for the disorder (cumulative evidence from the literature indicates winter and early spring as the period when most schizophrenic births occur).

This study, comprising 187 patients (117 males and 70 females under 40) who fully met the DSM–III–R criteria for schizophrenic disorder (American Psychiatric Association, 1987), showed considerable differences in familial predisposition to schizophrenia in the two seasonal groups. Five of the 84 patients born in the winter and early spring (6%), and 17 of the 103 patients born in the other months (16.5%) had a family history of schizophrenia ($\chi^2=4.9$, $P=0.025$). Furthermore, morbidity risk data confirmed the role of family history. Five of the 241 age-adjusted relatives of the probands born between December and April (age adjustment according to Weinberg's abridged method) and 18 of the 323 age-adjusted relatives of the probands born during the remainder of the year turned out to be schizophrenics ($\chi^2=4$, $P=0.043$), so that the latter group had a familial morbidity risk (5.3%) 2.65 times greater than that of the former (2%).

Consequently, our findings are apparently compatible with previous hypotheses of a lowered familial loading of schizophrenia among patients born in the winter and early spring, but manifestly differ from those of Drs Baron & Gruen. Undoubtedly, the lack of complete comparability of the protocols may have accounted for some of the differences in the results: for example, we used the end of April instead of the end of May as one of the benchmarks for separating the season of birth, and the Weinberg's abridged method instead of the more precise age correction based on continuous distribution of the ages at the disease onset. But we should not neglect the possibility that the samples selected in one or another or both of the studies are not completely representative of the phenomena under analysis. In fact, the figures for the secondary cases in our sample are somewhat inferior to those to be expected for relatives of Italian schizophrenics (Macciardi *et al*, 1987) and, on the contrary, the greater risk found by Drs Baron & Gruen (among the relatives of the patients born in winter and spring) apparently seems largely sustained by a few families with many cases of schizophrenia, i.e. by high-risk families. If this is true, then some of the discrepancies could be reconciled, given that systematic diathesis–stress interactions along a continuum of susceptibility are the bases for the seasonality phenomenon. Within this framework, we cannot only expect that the harmful effect of seasonal environmental factors is maximised when, as was apparently the case in our sample, the weight of familial predisposition to schizophrenia is in some way minimised, but also that the former further increases the likelihood of the schizophrenic disorder when subjects at high risk are predominantly considered.

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References

American Psychiatric Association (1987) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn, revised) (DSM–III–R). Washington: APA.

Macciardi, F., Provenza, M., Bellodi, L. *et al* (1987) Genetic notes of schizophrenic disorders. In *Etiopathogenetic Hypotheses of Schizophrenia: The Impact of Epidemiological, Biochemical and Neuromorphological Studies* (eds C. L. Cazzullo, G. Invernizzi, E. Sacchetti, *et al*), pp 21–32. Lancaster: MTP Press.

Machon, R. A., Mednick, S. A. & Schulsinger, F. (1983) The interaction of seasonality, place of birth, genetic risk and subsequent schizophrenia in a high risk sample. *British Journal of Psychiatry*, **143**, 383–388.

Torrey, E. F. (1987) Hypotheses on the seasonality of schizophrenic births. In *Etiopathogenetic Hypotheses of Schizophrenia: The Impact of Epidemiological, Biochemical and Neuromorphological Studies* (eds C. L. Cazzullo, G. Invernizzi, E. Sacchetti, *et al*), pp 41–48. Lancaster: MTP Press.

Antidepressant toxicity

Sir: I read with interest the review by Beaumont (*Journal*, April 1989, **154**, 454–458), and was surprised to note that there was no mention of the relatively new antidepressant fluvoxamine, which is reputed to be very safe when taken in overdose. Fluvoxamine inhibits the neuronal uptake of 5-hydroxytryptamine with little or no effect on the catecholamine system. Minor reported side-effects include: nausea, vomiting, dizziness, dyspepsia, headache, anxiety, palpitations, diarrhoea, and a rash (Roos, 1983; Classen *et al*, 1977).

There have been 42 cases of self-poisoning with fluvoxamine (Banerjee, 1988). One patient died, but necropsy showed the fluvoxamine tablets to be intact in the stomach, and the death was attributable to an overdose of propanolol. In another reported case, the patient was unconscious for five days, but recovered fully from her coma (Banerjee, 1988). The prolonged cerebral depression was thought to be due to a possible interaction between fluvoxamine and benzodiazepine metabolites. Thus it appears from the available data that fluvoxamine is relatively safe in overdose compared with the tricyclic antidepressants.

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References

BANERJEE, A. K. (1988) Recovery from prolonged cerebral depression after fluvoxamine overdose. *British Medical Journal*, **296**, 1774.

CLASSEN, V., DAVIES, J. E., HERTTING, G., *et al* (1977) Fluvoxamine, a specific 5-hydroxytryptamine uptake inhibitor. *British Journal of Pharmacology*, **60**, 505–516.

ROOS, J. C. (1983) Cardiac effects of antidepressant drugs. A comparison of the trycyclic antidepressants and fluvoxamine. *British Journal of Clinical Pharmacology*, **15**, 4355–4395.

Attitudes to anxiety

SIR: We are grateful to the late Dr Kraupl Taylor (*Journal*, May 1989, **154**, 697–704) for his timely reminder that anxiety disorders are true psychiatric disorders rather than perjorative labels. The very first patient we saw after reading his article gave such a clear example of this prejudice that we felt moved to write.

Case Report: The patient, a 34-year-old married white male labourer, presented to our anxiety disorders clinic with a five-year history of panic attacks and generalised anxiety. The severity of his illness may be judged from his opening statement: "If you can't help me then I'll have to jump off the [Clifton Suspension] bridge". The onset of this disorder was in 1984, with a sudden, spontaneous, severe panic attack. He immediately took a taxi home, but during the journey diverted it to the local casualty department. The principal symptoms he described were bilateral chest pain and paraesthesiae. He was examined and was "reassured" that his symptoms were only due to anxiety.

He remained disabled, despite relaxation training, for 2 years, and was reassessed in 1986 by a cardiologist for continued episodes of faintness and chest tightness. This consultant's view was that there was no evidence of heart disease, and he stated that "the right policy was to reassure him strongly in the hope that they [the panic attacks] would go away". He was subsequently prescribed diazepam by his GP. However, because he was frightened of becoming addicted, he did not take the drug. Following this he was prescribed propranolol, which he found ineffective. He has continued to suffer, and his continued employment has been jeopardised by frequent absences from work caused by panic attacks.

This case serves to emphasise how underestimation of the personal suffering caused by anxiety may lead to inadequate treatment, and potential damage to family life and employment. In the light of this and the many other examples we have seen, we strongly support Dr Kraupl Taylor's point of view. We suggest that the present negative attitudes towards the illness concept of anxiety and the consequent anti-benzodiazepine climate of opinion causes much extra suffering for those people least able to tolerate it.

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The epileptic arsonist

SIR: The recent article by Carpenter & King (*Journal*, April 1989, **154**, 554–556), makes compelling reading. The association between epilepsy and arson is a fascinating one, and we would like to describe a further case seen recently in our unit.

Case Report: Ms B, a 26-year-old woman, was referred to our unit following an incident in which she set fire to a shop in her locality. This was one of a series of fires set by this lady, and she had received a diagnosis of personality disorder at another psychiatric institution. The patient was initially maintained on chlorpromazine therapy, and during her stay she set another fire on the ward. Careful reassessment of her case revealed that her fire-setting behaviour occurred in response to "a male voice", which she heard intermittently. EEG studies were performed, and revealed gross abnormalities consistent with an epileptic focus in the temporal lobe. The patient was started on carbamazepine therapy, and her auditory hallucinations have ceased. She remains much more settled on anticonvulsants alone, and there has been no recurrence of her fire-setting behaviour.

This is another case of arson associated with epileptic activity. The excellent response to anticonvulsants has led to a change in the diagnosis in this patient. Unlike Drs Carpenter & King's case there was no evidence of alcohol use or brain injury in this patient's history. Her progress has been most encouraging. Her legal status is currently under review, and the diagnosis of epilepsy should have considerable bearing on the outcome of her case.

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Treatment of extrapyramidal side-effects

Sir: Fernando & Machanda (*Journal*, May 1988, **152**, 722–723) recently reported two cases of neuroleptic-induced extrapyramidal side-effects (EPS) (muscle rigidity and drooling) which were successfully treated with oral calcium. Both patients had EPS which persisted in spite of anticholinergic or antihistaminic agents (benztropine, procyclidine, or diphenhydramine).

We have completed three studies of the effects of the calcium-channel antagonists (CCAs) verapamil, nifedipine, and diltiazem on tardive dyskinesia, during which EPS were also rated (Reiter *et al*, 1989; Adler *et al*, 1988; Duncan *et al*, in preparation). Based on the report of Drs Fernando & Machanda, we assessed whether there was any increase in EPS after administration of the CCAs.

Methods were similar for all three studies. EPS were quantified by the Hillside/LIJ modification of the original Simpson/Angus EPS Scale (Simpson & Angus, 1970). EPS ratings were performed on alternate days over a 5–15 day period by a rater who did not know when treatment with CCAs was to begin. Each patient was rated by the same evaluator throughout the trial. Multiple ratings were made in order to blind the rater. All ratings were discarded except for those which were obtained immediately before treatment and on the last day of treatment.

Neuroleptics and all other medications were held constant for at least four days before, and throughout the course of treatment with CCA. Patients were excluded if they had any contraindications to CCAs (e.g. hypotension, cardiac conduction delays or block) or cardiovascular illness requiring medication.

CCAs were prescribed by physicians who did not rate the patients. The initial doses of CCAs were: verapamil, 160 mg/day; diltiazem, 120 mg/day; or nifedipine, 30 mg/day. For those patients who did not develop hypotension or bradycardia the dose was increased to: verapamil, 320 mg/day; diltiazem, 240 mg/day; or nifedipine, 60 mg/day.

Nine schizophrenic patients were treated with verapamil (mean maximal dose = 231 mg/day; s.d. = 84.3) for 2–5 days. Twelve patients (schizophrenia, 10; bipolar, manic, 2) received diltiazem (mean maximal dose = 195 mg/day) for 4–12 days. Nifedipine was administered to eight schizophrenic patients for 7–14 days; all patients received 60 mg/day. Patient characteristics have been presented in more detail previously (Adler *et al*, 1988; Reiter *et al*, 1989).

Statistical analyses were performed by paired Student's *t*-tests (two-tailed) on total Simpson/Angus EPS scores (items 1–9) at baseline v. scores on the last day of treatment with maximal dose of CCA.

No significant effects were observed on EPS after any of the CCAs (all $t<1$). EPS scores were unchanged from a mean of 3.1 ± 2.5 at baseline to a mean of 2.8 ± 2.0 after verapamil ($t(8)=0.71$, NS). EPS was also unchanged after diltiazem (mean at baseline $=3.5\pm3.3$, mean after diltiazem $=3.2\pm2.8$; $t(11)=0.65$, NS) and after nifedipine (mean at baseline $=2.1\pm2.1$, mean after diltiazem $=2.0\pm1.6$, NS). No clinically apparent changes in EPS were observed in any of the individual patients.

Our findings of an absence of effect of the CCAs verapamil, diltiazem, or nifedipine on EPS in no way contradicts the reported improvement in EPS after administration of calcium. Calcium may affect EPS via mechanisms different from those which affect cellular gating or intracellular calcium concentrations. Nonetheless, Drs Fernando & Machanda's findings might lead one to predict that CCA treatment would increase the mild EPS that our patients showed at baseline; this was not observed.

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References

Adler, L., Duncan, E., Reiter, S. *et al* (1988) Effects of calcium channel antagonists on tardive dyskinesia and psychosis. *Psychopharmacology Bulletin*, **24**, 421–426.

Reiter, S., Adler, L. & Angrist, B. *et al* (1989) Effects of verapamil on tardive dyskinesia and psychosis in schizophrenic patients. *Journal of Clinical Psychiatry*, **50**, 26–27.

Simpson, G. M. & Angus, J. W. S. (1970) A rating scale for extrapyramidal side-effects. *Acta Psychiatrica Scandinavica*, **Suppl. 212**, 11–19.

Spontaneous orgasms – any explanations?

Sir: I should like to report an unusual sexual problem.

Case Report: A 45-year-old muslim mother of three, who had been widowed three years earlier, complained bitterly of repeated, uncontrolled orgasms. These occurred up to 30 times per day without any sort of sexual contact. Her social functioning was severely impaired and she stopped practising her regular religious rituals and visiting the holy shrines.

She was referred for psychiatric opinion by a consultant gynaecologist who could find no physical cause for her complaint. I could find no psychological disturbance apart from the presenting symptom and consequent feelings of depression. FSH, LH, serum prolactin, testosterone, oestrogen, and progesterone were all within normal limits. The aetiology remains unclear.

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A HUNDRED YEARS AGO

The Suicide of Rudolph, Crown Prince of Austria

Since the suicide of the King of Bavaria, another tragedy has called the attention of the world to the delirium of Princes. Apart from the irresistible interest which men take in the fate of those exalted in rank, there is another reason why the insanity of Kings should become an object of serious study. It is only by availing ourselves of the lives and deaths of regal and princely families that we can trace hereditary disease backwards through many generations so as to arrive at some safe generalisation. It is, therefore, proper that there should be in this Journal an account of the recent suicide of the Crown Prince of Austria, viewed in those aspects which are especially interesting to us as students of mental disease.

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... But how can we conceive the heir of the Austrian Empire, a young man of thirty, to be in a condition so utterly forlorn that he could thus rush away from all his splendid prospects because he could not get a divorce from his wife in order to marry a mistress of whose heart and person he was already the possessor?

Everything made smooth for him from childhood, servilely flattered by the creatures who go about Courts, all his wishes anticipated, all his caprices gratified, the Prince, who now, perhaps, for the first time felt the full force of a love passion, was suddenly brought to face a limitation to his power and a check to the flow of his dearest wishes. This produced a revulsion of feeling, the wild intensity of which the one brought up amongst the losses and crosses of the world cannot conceive. One lesson the princes of Europe might learn, and that is to give up these close, dynastic marriages, which, instead of producing a race fitted to rule over men, seem calculated only to perpetuate and intensify hereditary diseases which exist in every princely family in Europe.

Reference

Journal of Mental Science, April 1889, 35, 72–74.

Researched by Henry Rollin, Emeritus Consultant Psychiatrist, Horton Hospital, Surrey

British Journal of Psychiatry (1989), **155**, 271–273

Books Reconsidered

Psychopathic Personalities: Kurt Schneider*

The first edition of *Psychopathic Personalities* appeared in 1912, roughly ten years after Jaspers' *General Psychopathology* and the last edition of Kraepelin's *Textbook of Psychiatry*. Schneider's role in applying Jaspers' method of psychopathological study to Kraepelin's classification of psychiatric disorder has been seen as an important aspect of his work (Hoenig, 1982) and is evident in his own *Clinical Psychopathology* (Schneider, 1959). However, his study of the classification of psychopathic personalities, an area which Kraepelin never succeeded in delineating clearly (Lewis, 1974), is regarded as his most important contribution (Anderson, 1959; Hoenig, 1982).

When I began to study Schneider's work, about 15 years ago, I was encouraged by my mentors to use the term 'personality disorders' rather than 'psychopathic personalities', and this has become a habit, so that in what follows I have used the two terms as if they were synonymous. Having no German, I am naïvely unaware of any nuances which may have been lost in the process and can only hope that I am not doing Schneider a disservice. I have been unable to discover when, or by whom, the substitution was first made. Certainly, the term psychopathic personality is obsolescent in English, its use now being more or less confined to mental health legislators and to psychologists working in the forensic field. Even among these groups, there is growing opposition to its use (Blackburn, 1988).

Werlinder (1978) has provided an account, in English, of the first edition of *Psychopathic Personalities*. The ninth edition (Schneider, 1950) was translated by Marion Hamilton. The two presentations are similar, suggesting that Schneider's views did not alter much during the lifetime of the work. Furthermore, Hamilton acknowledged the help she received from W. Mayer-Gross and E. W. Anderson, both of whom were familiar with Schneider's teachings. Therefore, it is likely that her translation of the ninth edition provides a representative account of the views which Schneider expressed during his career. Werlinder reveals that some criticisms of Schneider were made in the interval between the publication of the ninth edition and the appearance of Hamilton's translation. Although the criticisms were sufficiently serious to prompt a response from Schneider (1958), who by then had retired, they are not often discussed in English texts.

Psychopathic Personalities is in two sections. The first deals with issues of general importance, including definitions of key concepts, while the second provides descriptions of what Schneider considered to be the important types of personality disorder which were encountered in clinical practice.

To Schneider, 'personality' was a word used to convey someone's uniqueness, including his or her individual feelings and goals. It should be described in psychological terms, although it does not include the attributes usually referred to as 'intelligence'. Personality was normal if the subject was more or less average in comparison with others with the same cultural background. So-called 'abnormal personalities', by contrast, were variations on this "broadly conceived range of average personality" (p. 3). Such variations represented excesses or deficiencies in a statistical sense, and judgement of good or bad was "immaterial".

This definition of abnormal personality enabled Schneider to achieve his objective of introducing a way of describing personality disorders which was not judgemental. However, Schneider's critics claimed that he returned to a judgemental position when he went on to define such (personality) disorders as those "abnormal personalities who either suffer personally because of their own abnormality or make the community suffer because of it". Such criticism was unfair, because Schneider left no doubt that he believed that: "psychopathy lies in the degree to which the abnormality of personality afflicts the individual, not in the amount of social friction which may be engendered around him." (p. 3).

Schneider's definition of personality disorder was intended to establish which area, in what would otherwise be a very large field, was of concern to psychiatry – a gesture which would surely be appreciated by today's politicians and managers of mental health services! On a more serious note, I wonder whether it holds the key to understanding the discrepancy between the rates of psychiatric disorder (including personality disorders) which are reported by clinicians and researchers using structured interviews?

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*London: Cassel (1958). Translated by M. W. Hamilton.

In both sections of *Psychopathic Personalities*, Schneider discussed at length the relationship between personality disorder and other forms of mental illness. He confessed to finding it difficult to apply the medical model to *any* psychiatric disorder, since patients are often unperturbed by their experiences. However, it seemed reasonable to him that the concept of illness be introduced if mental changes occurred which could best be explained by a disease process. He thought it inappropriate to refer to psychopaths as "ill", because they did not meet this criterion, although to buttress this argument he removed from the category patients with disturbed behaviour resulting from diseases such as encephalitis.

It is often overlooked that Schneider emphasised the limitations of the diagnosis of a personality disorder. Typologies of such disorders were, he claimed, no more than descriptions of people, conceived within a professional relationship and inevitably incomplete. He was also strongly opposed to attempts at classifying personality 'systematically', by referring to 'structural' models. In his opinion such classifications failed to depict the types of patients encountered in the clinical setting.

Nevertheless, Schneider believed that it was important for psychiatrists to take into account those stable characteristics of patients which were conveyed by concepts such as personality and personality disorder, especially in cases of neurosis. While not liking the term neurosis, he paid considerable attention to individual neurotic symptoms which, to a greater extent than most modern psychiatrists, he saw as intrinsic features of personality disorders.

In the second section of the book, Schneider presented his own, unsystematic, typology of personality disorders. The equivalent terms in English for his ten types are (following Hamilton's translation): hyperthymic, depressive, insecure (with sensitive and anankastic subtypes), fanatic, attention-seeking, labile, explosive, affectionless, weak-willed, and asthenic. For each type he provided a description and a background review, including such things as genetic studies, differential diagnosis, and social impact. There is a high degree of internal consistency in these accounts.

Although it has been difficult to devise an approach to diagnosis which does justice to Schneider while at the same time addressing present-day concerns about reliability, some evidence of the validity of the typology has been found (Standage, 1977). It was also observed that there were relationships between diagnoses made within Schneider's classification and DSM–III (Standage, 1986).

The most frequently expressed criticism of Schneider is that he negated the role of psychotherapy. However, this is not apparent on reading *Psychopathic Personalities*. There, he simply commented that psychotherapy might not be very effective for patients with personality disorders and that such disorders should be taken into account when treatment was undertaken – not a very contentious opinion by today's standards! A more valid criticism might be that he underestimated the role of intrapsychic and interpersonal factors as determinants of the behavioural patterns which are implied by the term 'personality disorder.' In particular, I am surprised that he paid so little attention to concepts of 'self', which I would have expected to emerge in a phenomenologically-oriented review of such disorders.

In fact, when I read the descriptions of the various personality types, I do not derive a strong sense of what it is like to be labile, affectionless, weak-willed, etc., and I can only speculate on the reasons for this, which must include my own defensiveness and lack of sophistication in phenomenology. I have to search for the phenomenological elements in the work, and I find it in such things as the attempt to distinguish form from content, the emphasis on individual, meaningful data being required to put flesh on the skeletal typological diagnosis, and the need for the clinician to question the ways in which, say, an attention-seeking personality seeks attention.

Schneider appreciated that his personality types overlapped, but he did not recognise that the reliability of such a method of diagnosis would be low. If he had access to the modern literature, which indicates that there is a strong affinity between psychometric measures and clinical concepts, in spite of the efforts of psychiatrists and psychologists to prove otherwise, I wonder whether he would be quite so negative about systematic classifications, which lead naturally to a dimensional approach and thus to improved reliability? Such an approach would be consistent with his definition of abnormal personality.

Another criticism which might be made of Schneider today is that, although he paid a lot of attention to the relationship between personality disorders and the endogenous psychoses, he did so only in terms of "either/or." It has now become conventional to consider these conditions on *separate* diagnostic axes, as exemplified in DSM–III (American Psychiatric Association, 1980). It may be that Schneider wanted to promote the view that, in general, personality disorders and psychoses are qualitatively distinct from one another, in contrast to that which sees them as intermediaries between the latter and 'normality'.

Perhaps the most remarkable thing about *Psychopathic Personalities* is that the issues presented in it are still the major ones in the field of personality disorder. This makes it an excellent postgraduate text.

As criticism continues to be expressed about the diagnosis of personality disorders, it is salutary to remind oneself that Schneider set out to replace Kraepelin's socially valuing descriptions of such patients with a classification which was non-evaluating, psychological, and clinically relevant. Much work is still needed to determine the importance of personality in general psychiatry. Certainly, the treatment provided for patients with personality disorders needs to be improved – an undertaking that will derive little impetus from Schneider's rather sardonic comments (my favourite is the advice to stay out of the way of labile personalities on their bad days!). However, those who follow Schneider's approach to the definition and description of such disorders should at least remain free of allegations of prejudice.

References

ANDERSON, E. W. (1959) Preface. In Schneider (1959).

AMERICAN PSYCHIATRIC ASSOCIATION (1980) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn) (DSM–III). Washington, DC: APA.

Blackburn, R. (1988) On moral judgements and personality disorders. The myth of psychopathic personality revisited. *British Journal of Psychiatry*, **153**, 505–512.

Hoenig, J. (1982) Kurt Schneider and Anglophone psychiatry. *Comprehensive Psychiatry*, **23**, 391–400.

LEWIS, A. (1974) Psychopathic personality: a most elusive category. *Psychological Medicine*, **4**, 133–140.

SCHNEIDER, K. (1950) *Die psychopathische Personlichkeiten* (9th edn). Wien: Franz Deuticke.

—— (1958) Der Psychopath. *Fortschritte der Neurologie-Pyschiatrie*, **26**, 1–6.

—— (1959) *Clinical Psychopathology* (trans. by M. W. Hamilton). New York: Grune and Stratton.

Standage, K. (1977) *The Diagnosis and Classification of Personality Disorders*. PhD thesis. Newfoundland: Memorial University of Newfoundland.

—— (1986) A clinical and psychometric investigation comparing Schneider's and the DSM–III typologies of personality disorders. *Comprehensive Psychiatry*, **27**, 35–46.

WERLINDER, H. (1978) *Psychopathy: a history of the concept*. (Uppsala Studies in Education). *Acta Universitatis Upsaliensis*, **6**.

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Book Reviews

Editor: Sidney Crown

Current Issues of Suicidology. Edited by H. J. MOLLER, A. SCHMIDTKE and R. WELZ. Berlin: Springer-Verlag. 1988. 481 pp. DM 178.

Brought together under this single cover are some 60 papers that were presented at the first European symposium on Empirical Research into Suicidal Behaviour, together with some specially prepared for the book itself. The symposium was held in Munich, in collaboration with the German Society for the Prevention of Suicide.

The papers are presented in five different sections, concerned with epidemiology, clinical course and prediction, biological factors, psychosocial variables, and treatment evaluation. Contributors came mainly from the German-speaking countries and Scandinavia, with a small number from other European countries and the USA. Notable are some interesting presentations by workers from Hungary and Yugoslavia

This is clearly a record of what transpired at the symposium, and the papers appear to have remained essentially unchanged from the original verbal presentations. This means that the text is not easy to read as a continuous whole. While all the papers follow a standardised format, variations in style and use of English can in places render precise meanings difficult to decipher, although in the main this is no more than a minor problem. In places the data presented in discussion did not appear in the reported results, and the quality of bibliography varies a great deal from one paper to another.

Nevertheless, the value of this book is undoubted. At the very least it should stimulate communication between researchers in the various European countries, and it testifies to the vigour which characterises current European research in the field of suicidal behaviour. This is all the more remarkable when one reflects on how difficult it is to demonstrate whether or not preventive and intervention strategies have any effect at all. Such factors as low base rates, poor compliance, and complexity of multifactorial causation all conspire to make research in this area potentially unrewarding.

Personal research interests will of course dictate individual responses to the various sections of this book. But the wide range of approaches, from the biological to interpersonal and epidemiological considerations, should be warmly welcomed; the final section, which is concerned with treatment evaluation, will surely elicit universal interest and demand special comment. Workers associated with Muller at Munich feature prominently here, and the difficult problems of low compliance, heterogeneity of treatment strategies, and deficiencies in evaluation techniques are addressed in an impressive way. An important theme for further research emerges; we need to be far more discriminating with regard to all the complex variables involved before we can hope to arrive at any effective evaluation of our attempts to treat and prevent suicidal behaviour.

One surprising feature of this symposium is the fact that only one paper, that by Retterstol, is concerned with problems with regard to the nursing care of suicidal patients, although this is surely something that needs urgent attention in view of the increasing number of suicides in our psychiatric hospital wards. Perhaps this theme will be given more prominence in the next symposium.

Those with active research interests in the field of suicidal behaviour will find this book invaluable as a source of up-to-date information and statistics, as well as ideas for research development. Others will certainly want to use it for selective reference.

H. G. MORGAN, *Professor of Mental Health, University of Bristol*

Anxiety in Clinical Practice. By ANDREW SIMS and PHILIP SNAITH. Chichester: John Wiley. 1988. 103 pp. £16.50.

The College's guidelines on the use of benzodiazapine medications (*Bulletin of the Royal College of Psychiatrists,* March 1988, **12,** 107–109) reflect the widespread concern among psychiatrists and general practitioners about the hazards of these drugs. Their previous widespread acceptance and apparent safety undoubtedly encouraged a rather offhand approach to the diagnosis and treatment of anxiety. Now that this complacency has been undermined, it is timely for publications to appear on the topic of anxiety. *Anxiety in Clinical Practice* is a small volume written chiefly for primary care workers – not only general practitioners, but also clinical psychologists, speech therapists, and social workers. It is felt it will also appeal to trainee psychiatrists and psychiatric nurses.

The introduction and the historical perspective are particularly informative, possibly reflecting the special interest of the authors. The anecdotes include the 18th century tomb inscription of Sarah Fletcher in Dorchester Abbey, whose "nerves were too delicately spun to bear the rude Shakes and Jostlings which we meet with in this transitory World. Nature gave way; She sunk and died a Martyr to Excessive Sensibility."

The book includes chapters on the biological, psychological and social aspects of anxiety. There is an appendix on assessment scales, and a final chapter on the management of anxiety. Bearing in mind the authors' intention to produce a practical volume, this section is disappointingly brief. However, it does include sections on explanation and motivation for change, relaxation and meditation, exposure to anxiety, restructuring of attitudes, and self-control.

This modest volume could well be recommended to psychiatry trainees on a topic of growing importance for both psychiatrists and general practitioners. I feel that supplementary reading would be required, particularly in the areas of panic disorder and post traumatic stress disorder. Nevertheless, the authors have achieved an admirable summary of this pervasive problem.

R. J. DALY, *Professor of Psychiatry,*
University College Cork, Ireland

Limit Setting in Clinical Practice. By STEPHEN A. GREEN, RICHARD L. GOLDBERG, DAVID M. GOLDSTEIN and ELLEN LEIBENLUFT. Cambridge: Cambridge University Press. 130 pp. £20.00.

The title of this book is slightly misleading; the book is more specifically about limit setting with difficult patients in psychotherapy (and to a lesser extent in general psychiatry). The authors state, quite rightly, that this subject is often neglected by teachers and supervisors, leaving trainee psychotherapists (and psychiatrists) at times overwhelmed and out-manoeuvred by their most severely disturbed patients, to the detriment of both parties.

There are chapters covering the art and theory of limit setting, limit setting and the transference relationship, limit setting with in-patients, and finally teaching limit setting. Potentially destructive processes such as splitting, acting out, regression, dependency, and self-harm are outlined, and helpful ways of dealing with the more malignant aspects of these phenomena are described with the aid of clinical examples.

The chapter on transference will be particularly useful to trainees, as it includes an honest discussion of counter-transference feelings which can be aroused in the therapist, including hatred, aggression, and sexual arousal. That on limit setting with in-patients looks at both psychodynamic and behavioural aspects of the management of severely disturbed patients and the antitherapeutic responses which can be aroused in staff.

Treatment programmes need to be defined clearly and negotiated with staff and patient alike. Agreement on strategies for dealing with, for example, splitting, collusion, and acting out, whether originating with staff or patient, is essential, and a high level of understanding of unconscious mechanisms is demanded of ward staff.

This is a slim volume, but even so there is some repetition (presumably because the book has four authors). Nevertheless, it offers a clear practical introduction to limit setting, and is a useful source of reference on the subject. I recommend it for inclusion in the psychiatry/psychotherapy library.

STEPHEN P. REILLY, *Consultant Psychiatrist with Special Responsibility for Psychotherapy,*
Bootham Park Hospital, York

Homicide. By MARTIN DALY and MARGO WILSON. New York: Aldine de Gruyter. 1988. 328 pp. DM 72 (pb), DM 128 (hb).

"Why do people kill one another?" the authors ask. A thousand different reasons – we reply – it depends on which conceptual framework you apply. "Ah", say our authors, "we have a theoretical model that accommodates all the others; it is scientifically correct but it has been shamefully neglected for years". Sounds interesting, tell me more. "Well, it's called evolutionary psychology – sit back and this book will tell you all you need to know." Three hundred pages later, the theory remains hazy and its application to contemporary homicide seems tenuous.

Behavioural traits survive where they are valuable in ensuring abundant biological offspring; that, in a nutshell, is evolutionary psychology. Separate chapters cover the various forms of family homicide (e.g. killing of children, parents, and spouse), other types of homicide, and the criminal justice system. In each of them the authors purport to discuss the issues from the perspective of evolutionary psychology; often it is difficult to glimpse anything new in what they say. For example, they discuss the commonest form of urban killing: one drunken man killed by another during what Wolfgang back in 1958 called "an altercation of relatively trivial origin". That it is nothing new and that it is recognisable across different cultures, we already know. For the authors, however, "a capacity for controlled violence has regularly contributed to status" and "status has persistently contributed to reproductive success". Similarly, maternal infanticide is construed as the psychological trade-off between the mother's valuation of her baby and her valuation of her own remaining reproductive potential. Killing of a defective child and killing by a step-parent are analysed in predictable terms.

Although the authors claim to present science, they give us, in their words, a "general theory of human nature". Like most theories of human nature, this one is not written down. It generates no testable hypotheses, and where it doesn't fit properly you can bend it to shape. Books that address a complex subject such as homicide from a single perspective often become predictable and tiresome once the message has been put. Sadly, this one is no exception.

DEREK CHISWICK, *Consultant Forensic Psychiatrist, Royal Edinburgh Hospital*

Child Psychotherapy, War and the Normal Child: Selected Papers of Margaret Lowenfeld. Edited by CATHY URWIN and JOHN HOOD-WILLIAMS. London: Free Association Books. 1988. 405 pp. £30.00.

This timely publication is divided into two parts. The first is a scholarly account and critique of Lowenfeld's work within the history of 20th century developmental psychology, the child guidance movement, and psychoanalysis. Her life and experiences are set into intellectual context and presented as an explanation for the course that her thinking took. In the process, Urwin has illuminated and enriched our understanding of both.

Part II arranges the selected papers in chronological order, and into chapters by topic. An introduction to each chapter sets the papers in the overall framework of her life and work, and discusses the contemporary relevance of her ideas. The papers span 40 years of Lowenfeld's life (1890–1973), and reflect the mind of someone with wide-ranging life experiences. Lowenfeld began her professional life as a paediatrician with an interest in research, and ended it as one of the pioneers of child psychotherapy and a founder Fellow of the Royal College of Psychiatry. It is clear from these papers, however, that she never deviated from the belief in the importance of attending to the whole child; the physical, intellectual, and emotional status of a child must be looked at together and in the context of family ethos and culture.

The Children's Clinic, set up in 1928 and eventually renamed the Institute of Child Psychology, was her attempt to realise the aim to bring to the aid of the suffering child all knowledge which might have a bearing on his or her well-being. For those professionals who are interested in closer links between paediatrics and psychiatry, these papers may give fresh insight as well as impetus to provide a holistic approach to children's disease and suffering.

Fundamental to any treatment given to children is the language of communication used by the child and the physician. Lowenfold's paediatric background shows in her emphasis on seeing things from the child's point of view. This, coupled with her genius for invention, led her to develop communication tools for the child to use. Of particular interest is the world technique, which serves to demonstrate how physiology and emotion are bound up with cognitive processes and what the entire process might look like. For those professionals who wish to complement their psychodynamic understanding, or those who would like to try an alternative approach to their understanding of children, Lowenfeld's techniques and ideas will offer a worthy challenge.

Through the use of her non-verbal techniques, Lowenfeld developed certain ideas about children's thinking which she called 'protosystem thinking'. Unlike Freud's primary process, Lowenfeld's view was that this thinking operates multidimensionally within the totality and simultaneity of experience; although it has its own logic and laws, the conclusions are subjective and therefore idiosyncratic. This and other theoretical concepts were no more than working hypotheses. Given the need for fresh thinking in this area, it is to be hoped that the drawing together of Lowenfeld's insights in this publication will stimulate a revival of interest in her very original ideas.

THÉRÈSE WOODCOCK, *Senior Child Psychotherapist, Vale Drive Child and Family Psychiatric Service, Barnet, Hertfordshire*

Psychobiology and Psychopharmacology. Edited by FREDERICK FLACH. New York: Norton. 1988. 286 pp. £19.95.

This is the second in the 'Directions in Psychiatry' monograph series, which means that it consists of a collection of articles, in this case on psychobiological and pharmacological topics derived from presentations by 22 American authors to a continuing education programme of that name in the USA. The back cover claims, perhaps a little too immodestly, that the series offers "an essential body of knowledge for every professional involved in mental health care".

Certainly this volume could not be accused of simply presenting psychobiological research without an attempt to put such findings into a general psychiatric context. The introduction laments the polarisation produced by blinkered adherence by psychiatrists to one or other model of psychiatric disorder, and the early chapters on psychological and social aspects of psychopharmacological treatment, compliance problems, sexual side-effects of drugs, and combining pharmacotherapy and psychotherapy positively bend over backwards to allow a 'biopsychosocial' approach. Much of the content of these sections appears to derive from the clinical experience of the authors rather than empirical evidence, which may be an approach that is enjoyed by some readers. The remaining sections are the more expected reviews of a variety of psychobiological topics, ranging from updates on electroencephalography and scanning techniques, and on genetic research, to aspects of antidepressant and antipsychotic drug treatment, largely clinical chapters on the treatment of anxiety and the management of overdosage, and a final chapter describing the editor's own studies of visual defects in psychiatric patients.

It is difficult to think of a good reason to buy this book. Although homogeneity is attempted by prefacing chapters with an editor's summary, and although the volume on the whole scores on readability, it is a strange mixture of general clinical advice which borders on the commonsense or even homely, case histories, and reviews of clinical and research areas which with only a few notable exceptions are not comprehensive or well referenced. The heavy bias in review areas towards the American literature, and the inclusion in several sections on treatment of drugs not used in this country, would prove additional drawbacks for a trainee readership.

NICHOLAS SEIVEWRIGHT, *Consultant in Drug Dependence, Regional Drug Dependence Unit, Prestwich Hospital*

The Psychopathic Mind. By J. REID MELOY. Northvale, NJ: Jason Aronson. 1988. 474 pp.

There is no doubt that, as the policeman said, "We get every kind of kook in California". Many of them seem to pass through the Psychiatric Security Unit in San Diego's Central Gaol, where the author, a psychologist, works. Some of them figure in this book, along with other notoriously violent and sexually perverse men not personally known to the author, such as David Berkowitz ('Son of Sam'), Kenneth Bianchi (the 'Hillside Strangler'), Albert de Salvo (the 'Boston Strangler'), and the recently executed Theodore Bundy. Not all of the cases are multiple murderers, but many fuse sexuality and aggression in a peculiarly repellent way: one is tempted to say an American way, but it is a salutary reminder that this problem is not restricted to the United States that one of Meloy's patients is, or was before he killed himself, a Liverpudlian.

Psychiatrists dealing with very disturbed men will probably find the case histories, which are usually extensive, of interest. They are, however, highly slanted to fit in with the author's central preoccupation: that these men are not human. Some of the details that the author retells are so repugnant that the reader is inclined to go along with this view, but despite many attempts to do so, Meloy fails to justify it scientifically.

His style is to present himself as up-to-date with every aspect of the social and biological sciences. Kohutian self-psychology, psychoanalysis, attachment theory, neurophysiology, and neurochemistry all disclose, when reviewed by Meloy, a fundamental flaw in the make-up of his patients. The number of theoretical formulations becomes, in fact, an embarrassment. How do having a propensity to predatory as opposed to affective aggression, a reptilian brain, and a "predominate, archetypal identification with the stranger self-object ..." all fit with each other? Meloy advances each of them as explanations. His favourite seems to be the reptilian state which is supported by "the absence of perceived emotion in their eyes", but here a suspicion creeps in. The author seems to reason: psychopaths are inhuman, I cannot therefore relate my feelings to theirs, they have no feelings like mine, therefore they are inhuman.... Isn't this a bit circular?

Reading the book became a profoundly depressing experience. The words Meloy uses are unnecessarily portentous and technical, and they began to seem like weapons in Meloy's battle against beastliness. The patients' tendency to deceive Meloy and his colleagues seems symptomatic of the failure of words to provide a link between professional and patient. An account of the patients' society, which created them and presumably also related to them and found them human, is missing, and with it goes any possibility of replacing explanation with understanding.

I began to wonder whether 'psychopath' was any more informative a word than 'witch', and found this a sobering thought. Witchcraft was given a considerable boost by the Inquisition. What is psychiatry doing for psychopathy? Read this book if human depravity is one of your interests – but don't give it to your patients.

DIGBY TANTUM, *Senior Lecturer, Department of Psychiatry, University Hospital of South Manchester*

Current Topics in Neuroendocrinology Vol 9: Stimulus-Secretion Coupling in Neuroendocrine Systems. Edited by D. GANTEN and D. PFAFF. Berlin, Heidelberg: Springer-Verlag. 1988. 256 pp. DM 178.00.

This publication, which forms part of an extensive series in neuroendocrinology, presents eight contributions from centres in North America and Europe on various aspects of neuroendocrine secretory mechanisms. Much of the work described is based on the hypothalamo-neurohypophysial model, with additional complete chapters devoted to the molluscan model peptidergic neuronal system, simulated mathematical models of potential output from peptidergic fibres, and a detailed description of currently identified insect neuropeptides. The emphasis is predictably on electrophysiological aspects, with little attention paid to receptor-mediated signal transduction and intracellular events until the final chapter. This chapter, which deals with stimulus-secretion coupling in the pancreatic beta cell, seems somewhat misplaced in a text which does not appear to aim at comprehensive coverage of signal transduction as a whole. Although each chapter is informative and thorough in its own right, the lack of editorial overview means that this is inevitably a book for the specialist neuroendocrine physiologist. For psychiatrists, endocrine physicians, and neurologists the book is of interest for reference rather than essential reading.

J. P. MONSON, *Senior Lecturer, The London Hospital, Whitechapel*

CUTTA TRAL RARY

Clues: Investigating Solutions in Brief Therapy. By Steve de Shazer. London: W. W. Norton. 1988. 202 pp. $25.00.

This is a book to be recommended. It is relatively short, and clearly written. Its style might not strike a chord with those who are more at home with traditional psychoanalytic styles of writing. Nevertheless, the jargon which is used is usually adequately defined.

This book develops from a simple, single observation, namely that patients in their initial presentation often indicate to the therapist that their complaint, symptom, abnormal behaviour, etc. may not be entirely consistent; that it may be sometimes absent. This seeming commonplace forms the heart of the treatment approach. What the author develops around it is a rationale and course of action which aims to bring to the patient more opportunities for the symptom to fail to appear, and hence to achieve symptom removal.

The treatment approach is largely cognitive in style, but includes addressing issues to do with poor motivation. No obvious use is made of the concept of unconscious processes. This may not be a failing, however, and since the results of the treatment, at least in the hands of the author and his associates, is brief and particularly successful, the method merits the serious attention of other workers.

Kingsley Norton, *Consultant Psychotherapist, Henderson Hospital*

Family Evaluation: An Approach Based on Bowen Theory. By Michael E. Kerr and Murray Bowen. London: W. W. Norton. 1989. 400 pp. £22.00.

This is a book written by family therapists about a system of 'family evaluation' developed by Bowen, who was apparently influenced in formulating his ideas by two publications: E. O. Wilson's *Sociobiology* and P. D. MacLean's *Education and the Brain*. The reader is introduced to a variety of technical terms based on suppositions about how families function and how psychiatric disorders occur. The authors go to considerable lengths to justify their theoretical framework, reaching out into the realms of how the physical sciences as well as the biological sciences developed, which I believe will make the average reader uncomfortable. It is all very well for a populist writer to start with such fundamentals in describing how the double helix configuration of DNA was discovered, but when two American psychiatrists attempt to give this degree of significance to an esoteric form of clinical assessment, it comes over as pretentious. A blow-by-blow detailed historical account of how the system was formulated is provided, such as might be appropriate for Alexander Fleming discovering penicillin or Louis Pasteur carrying out the experiment which revolutionised medicine.

The author's recommended system of family evaluation is described in a book of about 180 000 words. A lot of assertions are made, particularly about how psychiatric problems arise, without reference to any hard evidence which would serve to support the views expressed. Considering the importance the writers appear to attach their own work, it is surprising how little solid backing in the form of references to the scientific literature are made. I would guess that the methods and ideas that they advocate which a family therapist would find useful would also be found in a more concise and cheaper *vade-mecum* on this subject. This book is not to be recommended either to individuals or libraries.

Ian Berg, *Consultant Child Psychiatrist, Department of Psychological Medicine (Children), Leeds General Infirmary*

The Hypothalamic-Pituitary-Adrenal Axis – Physiology, Pathophysiology and Psychiatric Implications. Edited by Alan F. Schatzberg and Charles B. Nemeroff. New York: Raven Press. 1988. 223 pp. $61.50.

This volume arises out of a symposium held at the Annual Meeting of the American College of Neuropsychopharmacology in Hawaii in 1985. Because of the rapid evolution of this field, contributors have included in their chapters new data beyond those presented at the symposium. The contributors are all American biological psychiatrists, and the book reflects both the strengths and weaknesses of that group and the advantages and disadvantages of books originating from meetings.

The main focus of the book is the role of corticotrophin-releasing factor (CRF) in the production of hypercortisolaemia in depression. CRF was isolated from the hypothalamus, but it is now known to have an extensive but discrete CNS distribution. The peptide is increased in the CSF in depressed patients, and when it is administered to animals there are a number of interesting behavioural effects. There is no doubt that this is a fascinating area of neurobiology – the so-called 'new neuroendocrinology'. It seems likely that CRF is an important mediator of the behavioural response to 'stress'. The authors of several chapters link these observations and go on to suggest that CRF hypersecretion is important in the genesis of depressive disorders. However, in their enthusiasm these authors seem to have forgotten that many depressed patients do not exhibit hypercortisolaemia and that the clinical associations and specificity of the DST are far from clear. Moreover, in many chapters it appears that chronic stress is seen as the equivalent of depression.

A scholarly chapter from Sopolsky & McEwen puts forward the notion that the raised steroids found in depressed patients and Alzheimer-type dementia patients may be deleterious and that cognitive changes may follow from the associated hippocampal damage. Again, the undoubtedly interesting neuroscience outweighs the supporting clinical evidence.

The book is uneven in style and form. Some chapters are overviews; others present detailed studies and data. There is much overlap and repetition, particularly of the background outlined above. It is difficult to see whom the book is aimed at, but it could be recommended for the dedicated researcher in this area. Despite all these caveats, the authors have the courage of their convictions and a large number of testable hypotheses are generated, and that can't be bad.

I. N. FERRIER, *MRC Clinical Scientist, MRC Neurochemical Pathology Unit, Newcastle General Hospital, Newcastle upon Tyne*

Handbook of Cognitive-Behavioural Therapies. Edited by KEITH S. DOBSON. London: Hutchinson. 1988. 426 pp. £30.00.

The 'cognitive revolution' in psychology started in the 1960s, and since that time there has been an explosion in the published literature on the theory and clinical efficacy of cognitive-behavioural approaches. For those at the forefront of research in this area it is an exciting time. However, for others, attempting to come to grips with current developments in this field can be both frustrating and confusing. At what point does a behavioural approach merge into a cognitive behavioural approach? Are there any 'pure' cognitive therapies, or do all of them incorporate some behavioural techniques? Dobson takes as his starting point a broad definition of cognitive behavioural therapies: all those approaches that assume a primary role for cognitions in determining emotional and behavioural responses to events or experiences. This shapes the framework of the text and allows a comprehensive overview to be given of a wide range of theoretical models and clinical interventions.

The list of authors (including Beck, Ellis, Rehm, and Shaw) is impressive, and their contributions are of an excellent standard. The chapters not only address clinical and research issues, but clearly outline the philosophies underpinning the different approaches. The book is divided into three sections, covering the development of cognitive behavioural therapies and issues in cognitive assessment, the therapies available, and lastly an overview and analysis of future developments in the field.

In the preface Dobson writes that the impetus to producing this book came from having to teach about the theory and practice of cognitive therapies. He states that when he sought a "succinct, comprehensive handbook of the field of cognitive behavioural therapies" none was available. I can pay the editor no higher compliment than to say that that gap has now been successfully filled by this textbook. I cannot recommend it strongly enough to all those with an interest in the philosophy and practice of these approaches.

JAN SCOTT, *Consultant and Senior Lecturer in Psychiatry, University Department of Psychiatry, Newcastle upon Tyne*

Treatments for the Alzheimer Patient. Edited by LISSY JARVIK and CAROL HUTNER WINOGRAD. New York: Springer Publishing Company. 1989. 272 pp.

This is a good text: USA-centred, but of wider interest and usefulness. There are four sections: clinical care, family and community interventions, policy (very exclusive to the United States), and research. Appended are a variety of rating scales, including several which are much used, and details of (American) helping organisations and of some relevant publications. The references too are largely American, with omissions of important British work on the supporters of the demented by Gilleard, Gilhooly and others. The section on research is somewhat thin, and scarcely does credit either to the complexity of the growing volume of epidemiological research, or to the sophisticated analysis of burden for supporters and of specificity of interventions. Work by Zarit is too curtly summarised as "care giver problems progress as the duration of Alzheimer's disease lengthens". On the other hand, the opening chapter on 'The physician and the Alzheimer patient' by Winograd is admirable, setting out a broad-fronted approach with a nice attention to practical details (although the author, in discussing investigations, ducks the thorny question of how intensively the very aged 'typical' Alzheimer patient should be investigated).

Jarvik's chapter on 'Reviewing the future prospects for research' is characteristically wise and well-informed. This is a sensible, practical book, more likely to be bought by individual readers in America, but well worth adding to some British libraries.

TOM ARIE, *Professor of Health Care of the Elderly, Nottingham University*

X-Linked Mental Retardation 3. Edited by JOHN M. OPITZ, GIOVANNI NERI, JAMES F. REYNOLDS and LAVELLE M. SPANO. New York: Alan R. Liss. 1989. 707 pp.

This large book is the proceedings of the 3-day Third International Workshop on Fragile X and X-Linked Mental Retardation, held in Italy in 1987. The contents have previously been published in *The American Journal of Medical Genetics* in 1988. The book is dedicated to

Martin and Bell, who have both died in the past 10 years and whose names are associated with one variant of the fragile X syndrome.

Some papers are given in full and some in abstract form. The wordprocessor style of print does not make for easy reading. The lists of participants and contributors and the bibliography are formidable.

The content of the book is highly specialised and hard to read unless the reader has a background knowledge of the subject. For the clinician the first section, on clinical studies and nosology, is the most relevant but I could find only one reference to psychiatric sequelae, namely that a link has been suggested between autism and the fragile X syndrome.

As a clinician and not a "syndrome hunter", I was pleased to be updated on the physical and developmental findings. It has often been said that the physical signs are minimal (other than macro-orchidism in some), but many papers provide evidence of the wide range of abnormal features in this syndrome and possible links with such diverse conditions as sudden infant death, heart abnormalities, and a predisposition to unusual cancers. I was also unaware that the presence of a fragile X site may predispose to non-disjunction of other chromosomes.

This is a book for research workers rather than clinicians, for those who wish to become familiar with a range of syndromes and for those who have a specific question to answer.

JOAN BICKNELL, *Professor of the Psychiatry of Mental Handicap, St George's Hospital Medical School, London*

Cognitive-Behavioral Therapy with Families. Edited by NORMAN EPSTEIN, STEPHEN SCHLESINGER and WINDY DRYDEN. New York: Brunner/Mazel. 1988. 392 pp. $37.50.

The aim of this book is to apply cognitive-behavioural principles which are well known for the treatment of individuals, to the treatment of families. In this, the book covers new ground. One of the editors is based in the UK, and most of the eleven authors are from the USA. The book has thorough subject and indexes, and an extensive list of references following each chapter.

The book starts with two chapters on theory and methods of cognitive-behavioural family treatments. These are clearly explained, and well illustrated with diagrams and tables. The remainder is dedicated to treatments of specific family problems. These cover a wide range of clients, from childhood problems (e.g. child physical abuse) to marital problems (e.g. physical aggression), to problems with elderly family members. These chapters are written with the clinician in mind. They provide useful examples and case vignettes explaining both the theoretical framework and the practical applications.

I would have found more use of tables and diagrams in the treatment chapters helpful. I would recommend the book to those in either family therapy or cognitive-behavioural therapy with individuals, who want to expand their clinical armamentarium.

C. M. ABSOLON, *Senior Registrar in Child Psychiatry, The London Hospital, Whitechapel, London E1 1BB*

Textbook of Psychiatry. Edited by JOHN A. TALBOTT, ROBERT E. HALES and STUART E. YUDOFSKY. Washington: American Psychiatric Press (distributed in the UK by the Cambridge University Press). 1988. 1324 pp. £40.00.

The goal of this volume is to provide a textbook that is practical as a primary reference for psychiatrists, psychiatrists in training, other medical specialties, associated paramedicals, and medical students. I do not believe it will achieve that status on this side of the Atlantic as the clinical section is fashioned around the cornerstone of DSM–III–R, which is naturally more familiar and essential to practitioners in North America. However, this should not detract from the value of this textbook, which has much to recommend it.

It contains 38 chapters, with 61 contributors, all experts in their own fields, and the editors are to be congratulated for limiting repetition, a feature of other multi-author textbooks, to a minimum. The volume is divided into five sections: 'Theoretical foundations', 'Assessment', 'Psychiatric disorders', 'Psychiatric treatments', and 'Special topics'. There are two appendices, one on diagnostic criteria from DSM–III–R and one on excerpts from the American Psychiatric Glossary. Psychiatrists from these islands, particularly those interested in research, will find the DSM–III–R criteria invaluable. There is an excellent up-to-date list of references at the end of each chapter, although there is a natural bias towards North American authors. The editors have obviously taken great trouble in trying to standardise the contributions from the various authors, and in this they have been successful – too successful in some cases, particularly in the section on psychiatric disorders, which tends to become monotonous at times, following the format of DSM–III–R rather rigidly.

The section on theoretical foundations has a good up-to-date overview on genetics in relation to psychiatry. The chapter on normal growth and development is well worth reading, and covers the work of all major contributors in this field. Some of the language is rather technical in places, for example "ontogeny recapitulates phylogeny". The evolution and development of psychoanalysis and the later psychodynamic school is well documented, particularly with reference to the theories of Freud.

In the section on assessment there is a very informative chapter on 'Laboratory and other diagnostic tests in psychiatry'. This includes a short description of current brain-imaging techniques such as magnetic resonance imaging, positron emission tomography, and regional cerebral blood flow.

The section on psychiatric disorders is generally of a high standard, although there are some deficiencies. There is an excellent contribution on schizophrenia, with a comprehensive review of the epidemiology and aetiological theories. The chapter on anxiety disorders is to be recommended, particularly the contributions on panic disorders and post-traumatic stress disorder. There are some interesting personality disorders, such as "avoidant personality disorder" and "self-defeating personality disorder". Whether these concepts will cross the Atlantic remains to be seen. I was disappointed in the contribution on alcohol dependence/alcohol abuse. There is no mention of the famous Rand reports; nor is there any discussion about the current thinking on 'controlled drinking'.

The section on treatment was fully comprehensive and reflected some of the medico-legal constraints in the USA. The psychotherapies are particularly well covered. In the 'Special topics' section I would recommend the contributions on suicide, ethics and community care. I was fascinated to read that Nevada has one of the highest suicide rates in the United States. Could this have anything to do with the casinos? There is a good review of community care in the United States, and the author makes the valid point that "the dollar does not follow the patient". In other words, when the patient moves out into the community few resources move with him. It was a pity that little reference was made to the international scene, such as the Italian experience.

Overall, this is an excellent textbook of psychiatry which certainly should meet the editor's goals and expectations. Psychiatrists on this side of the Atlantic will find it an invaluable up-to-date reference book. It is attractively bound and well laid-out, and is excellent value at £40.00.

WILLIAM J. DELANEY, *Consultant Psychiatrist, St Dymphna's Hospital, North Circular Road, Dublin*

Essential Papers on Countertransference. Edited by BENJAMIN WOLSTEIN. New York: Columbia University Press. 1988. 359 pp. $31.00 (pb), $69.00 (hb).

The centenary of Breuer & Freud's early observations of transference and countertransference in *Studies on Hysteria* will take place in 1995. The essays in this book could be said to celebrate that crucial discovery. Each essay has been selected to represent a significant change in the concept and clinical study of countertransference, and therefore in the evolution of psychoanalysis, between 1910 and 1983.

As a historical summary of the changes that have taken place in the concept of countertransference, Wolstein's first chapter is particularly helpful. He traces the development of new insights derived from the early and direct Freudian interpretive work on the patient's oedipal material, which excluded direct consideration of the countertransference, to the present variety of perspectives arising from the development of ego psychology, object relations, interpersonal relations theories, and the exploration of the transference and countertransference in self-psychology. His final chapter on the pluralism of perspectives on countertransference, a subject of considerable evolutionary interest and complexity, I found at times to be somewhat labrynthine. One of the issues he affirms, as I understand it, is that with the move from an id to an ego interpersonal model of psychoanalysis, the patient who has been helped by a psychoanalyst to work through his transference problems may benefit by explicitly facing the psychoanalyst with what he considers to be his psychoanalyst's own countertransference distortions. The therapist at this point will have to decide whether to end therapy or to continue the exploration into his own assumed distorted perceptions (perceptions that had previously been accepted by his peers as objective and reality-based) in the hope that a further level of maturative development, whatever it may be, can be achieved for his client and possibly for himself. Wolstein's development of this view will, I imagine, evoke an interesting debate.

Between these two chapters lie 17 essays which move in a developmental sequence showing different points of emphasis. They make impressive and sometimes fascinating reading. They have been selected to typify the changes in the perception of countertransference over time, and include insights from Freud, Ferenzi and Rank, Reik and Clara Thompson, Racker and Searles, Winnicott, and Gill.

I can warmly recommend this book to all psychodynamically interested psychotherapists, and particularly those in training. Some may already have read a number of these essays, but most are of a calibre that benefit from a second or third reading.

BRIAN LAKE, *Honorary Consultant Psychotherapist, Department of Psychotherapy, St James's University Hospital, Leeds*

Feminist Counselling in Action. By JOCELYN CHAPLIN. London: Sage. 1988. 131 pp. £7.95.

The core of Chaplin's book is a systematic account of what she is trying to achieve as a feminist counsellor, how she defines the role, and how she prepares for different stages of the counselling relationship. She relates her values, aims, principles, and techniques to the processes and outcomes of counselling, using effective case illustrations.

She stresses the importance of demystifying and equalising the relationship, and discusses the influences of practicalities on people's lives and the need for external as well as internal change. A description of her way into the relationship, through unconditional acceptance, valuing defences and trying to understand what they represent, is followed by useful strategies and techniques for following clues "through the labyrinth". Symbolism of death and rebirth, and the rhythms of nature and personal and emotional life illuminate the stages and processes of growth. There is a particularly clear account of how assertiveness training can be used as an aid to change.

Chaplin's claim that her model of counselling respects and celebrates difference, rather than seeing it as concerned with superiority and inferiority and "divided split opposites", is largely sustained. Her association of mothering with the first stage of counselling I found problematic, though: it leaves unanswered questions about the power of mothers over children between counsellor and client. The association can also legitimise present expectations of female/male roles, rather than transcending them as the book aims to do.

Some theoretical problems and major debates in feminist theory are glossed over – such a short account cannot adequately address the complex nature of links between person and society and the relevance of an individualised model of counselling to different groups: female/male, black/white, and people of different class or culture.

Nevertheless the book is stimulating, leaving many ideas to reflect on. It gives a constructive account of the distinctive features of feminist counselling, as process and relationship.

NORMA BALDWIN, *Lecturer in Applied Social Studies, University of Warwick*

The Pluralpsyche: Personality, Morality and the Father. By ANDREW SAMUELS. London: Routledge. 1989. 253 pp. £12.95 (bp), £25.95 (hb).

It is difficult to summarise the message of this book, because it deals with a number of aspects of Jungian psychology which are rather separate; a result, perhaps, of the fact that some of the chapters have been published elsewhere. For those who know the papers the book is inevitable disappointing, especially since there is little adaptation – the phrase 'in this paper' even once appears.

Samuels deals, *inter alia* (as he would say, for there is considerable use of classical phrases, e.g. on p. 182: *hierosgamos, soror mystica, nigredo, prima materia, fermentatio, morteficatio*, and *putrefactio*), with alchemy, countertransference, the *mundus imaginalis*, the primal scene, and the feminine principle.

I shall discuss here the chapter on countertransference which, although a potentially important topic, highlights the weaknesses of this book for the general reader. It presents a fantastical and Jungian-derived account of the phenomenon with no attempt to persuade non-believers of its value or truth. To the sceptic it is almost meaningless. Samuels employs the concept of embodied countertransference in which the analyst becomes "part of the patient's inner world". To attempt to explain this, the notion of the *mundus imaginalis* is invoked, an *imaginalis* world shared by analyst and patient. Armed with this mystical concept, Samuels abandons normal logic: "As Buber says, in dance the whole world becomes subservient to the ecstatic soul. Analysis too is a form of dance..." Is it? I am not persuaded. Again, we find that it is important that the analyst should function as a mystic for the wider group of society, and that "analytical mysticism ... does not expend itself onanistically and nihilistically".

I think this gives the flavour of the book, which no doubt will appeal to Jungians. For those not totally committed, this book will not change their minds.

PAUL KLINE, *Professor of Psychometrics, Department of Psychology, University of Exeter, Devon*

Children Need Groups: A Practical Manual for Group Work with Young Children. By W. R. SILVEIRA, GILL TRAFFORD and ROSEMARIE MUSGROVE. Aberdeen: Aberdeen University Press. 1988. 134 pp. £8.50 (pb), £14.50 (hb).

In his foreword to this book, Professor F. Stone pays tribute to the clinical experience of the authors, and it is clear throughout what is essentially a straightforward, almost 'recipe book', approach to group work with young children that the authors have wealth of practical experience and sensitivity to children on which to draw. This makes this a uniquely useful text for those working with groups of children. Whatever their stage in training or experience, this book has useful guidelines and clear practical ideas, based on sound theory and a wide exposure to many children with different problems.

The book covers such basics as mother and toddler groups and how to set them up to the much more demanding specialised work with groups of sexually abused children. There are chapters on self-image, children at school, dealing with loss and handicap, children in hospitals, and residential schools. It considers the child as a member of the community in the widest sense, and examines different groups to which a child may belong. Each chapter begins with an introduction to the topic and is then subdivided into various sections. The chapter on handicap, for example, deals with trust, guilt, low self-esteem, and loss. Each section contains one or more exercises which can be used with a group of children to help to deal with this specific issue. The exercises are described and then followed by a number of conclusions which may be drawn from the results. In this way, a relative beginner to group work could use this book in order to enable themselves to tackle a wide range of children's problems with confidence. I was particularly pleased to read the helpful section on work with sexually abused younger children.

I found the book a pleasure to read. It is stimulating and helpful at the same time, and I would not hesitate to recommend it to anyone involved in, or contemplating, group work with young children.

SALLY E. BONNAR, *Senior Registrar, Department of Child and Family Psychiatry, Dundee Royal Infirmary*

Psychopathology and Differential Diagnosis: A Primer. Volume 1. History of Psychopathology. By HENRY KELLERMAN and ANTHONY BURRY. New York: Columbia University Press. 1988. 270 pp. $69.00.

This purports to be a history of our concepts of psychopathology. It is in fact 'psychopathology' used in a restricted sense, and 'history' limited to trace a rather narrow path. The book is divided into six parts. The first three – covering antiquity, the middle ages and the Renaissance and the modern world – are all explored with a view to demonstrating the antecedents to subsequent Freudian theory. Parts 4 and 5 are respectively on 'Nosological systems and the appearance of Sigmund Freud' and 'Typologies and followers of Freud'. The sixth part deals with contempory views: ego psychology and object relations. There is no mention of the origins of psychopathological thinking propounded by Jaspers, Schneider, Husserl, or Sartre, and there is no working through of the immense importance that biological advances have had on the understanding of psychopathology. It is unfortunate that the authors' view of history is restricted by psychoanalytic spectacles which tend to refract ideas explained by ancient writers into shapes which they would hardly recognise themselves. For example, the authors claim that the Old Testament frequently alludes to epilepsy and depression; however, reference to neither could be found in a substantial concordance. This book largely succeeds in its intention of relating ancient concepts to psychoanalytical thinking, and right from the beginning it introduces psychoanalytic concepts to 'explain' earlier theories. It is unfortunate that past cultures are labelled as irrational and unscientific without any apparent attempt by the authors to try and get inside the culture and inside the minds of the proponents of ideas.

There are various important routes to psychopathology that have not received mention in this work. For example, the association made by ancient Greek writers between cerebro-spinal fluid, semen, and the life force would seem essential for the history of psychoanalytic concepts. The point made by Norman Cohn so eloquently in *Europe's Inner Demons* that the persecution of witches only occurred at the end of the middle ages and in the early Renaissance period is missed by these authors, who ascribe the witch-hunt to medieval thinking. Unfortunately this history is excessively derivative, as there are only 17 references for the historical section and most of these are short historical summaries rather than original works. The history of psychopathology is a fascinating study. Unfortunately, this work will not answer most of the questions one would like to ask.

A. C. P. SIMS, *Professor of Psychiatry, University of Leeds*

Macmillan Dictionary of Psychology. By STUART SUTHERLAND. London: Macmillan. 1989. 491 pp. £29.95.

As Sutherland points out in his preface, psychology has become rife with complex concepts and technical terms. Nor is it free from the great importance of many other disciplines impinging on the science, such as sociology and neurochemistry. Reviewing such a comprehensive dictionary is never easy, because one is clearly limited in one's area of knowledge.

Having said this, I found this volume outstanding. It appears to cover all the major areas from the neurosciences, through mainstream psychology to psychoanalysis. It has a useful appendix providing diagrams of the brain, and throughout the text there are helpful illustrations. The definitions are helpful and clear, and Sutherland succeeds in giving more than definitions indicating also how concepts are used. The attention to detail is superb, and at times I found myself almost reading page for page. The problem here is that one is suddenly made aware of how much one does not know.

Although it is written for psychologists, this volume deserves to be found in any academic library. It will be extremely useful to psychiatrists as well as psychologists, and a paperback edition would certainly be worth personal purchase by students and practioners alike.

PAUL GILBERT, *Prinicpal Psychologist, Department of Clinical Psychology, Pastures Hospital, Derby*

Psychology For Medicine. Edited by T. W. ROBBINS and P. J. COOPER. London: Edward Arnold. 1988. 310 pp. £11.95.

This book is based on the pre-clinical course in psychology for medical students at Cambridge. Although each chapter is written by a different author, it is carefully constructed and edited to produce a coherent work. Despite being pitched at an elementary level, the book is of the highest critical quality and, particularly in its later chapters which move towards clinical practice, does much to dispel common myths and loose thinking.

The reader will be disabused, for example, of any notion that "stress can be responsible for most things" or that "because we understand rather little about psychology, anything which we don't understand must be psychological in origin". The distinction between factors which predispose to disease and those which exacerbate pre-existing conditions is made very clearly, while the section on intelligence also unties some old knots. The topics covered are wide-ranging, but do leave some gaps: perception and memory are covered, but the control of movement is mentioned only in passing; neuropsychology is described from a clinical viewpoint, despite the rarity of some of the conditions, but psychosis is scarcely mentioned, presumably because it is regarded as too clinical. What I find odd, though, is not so much the content of the book, which is excellent, as the presumed ignorance of the people for whom it is written. The topics covered in the book are all essential reading not only for doctors, but also for anyone who will have professional dealings with people as individuals, but the subject matter which is covered is by no means common knowledge. Psychology is, sadly, not a part of our education in the way that history or literature is. If this book goes some way to putting across a scientific approach at a simple level in a subject beset with easy answers then it will be a step in the right direction.

R. M. RIDLEY, *Division of Psychiatry, Clinical Research Centre, Watford Road, Harrow, Middlesex*

The Comforts of Madness. By PAUL SAYER. London: Constable. 1988. 128 pp. £9.95.

This short novel, in 22 terse sections, is an extraordinary achievement. More of a parable than a wholly realistic account, it charts the withdrawal of its young narrator from all human activities. The actions of those around him, relatives and professional carers, are recorded with painful precision.

At least, I hope it's a parable. The treatments he receives include the unorthodox and almost certainly the unethical. At one point he is told, "No-one can exist like you . . . there are no known cases". Yet he acts as a silent spokesman for many whose views on their 'illness' do not corresond with those who are 'treating' it. Reality is only just out of focus.

Despite its obvious qualities – craft, suspense, humour, and economy, to name just a few – it is surprising that such an offbeat novel should pick up major prizes like the Constable and the Whitbread. This success has resulted in much publicity for the author, a psychiatric nurse. There are similarities between the central figure of this novel and another fictional idiot savant, Dustin Hoffman's character in the Oscar-winning film *Rain Man*.

Why should such exotic manifestations of mental illness be given such a high profile? One answer could be that such characters are particularly intelligent and perceptive. Another might be that they keep the public mind off the closer reality of mental illness in its more mundane forms.

Sayer has written a splendid book. I hope we will hear much more from him, whether he chooses to express himself through fiction or by continuing to work for the mentally ill.

BERNARD INEICHEN, *Senior Research Fellow, Department of Performance and Standards, Newham Health Authority, London*

Psychopathology and Psychotherapy in Homosexuality. Edited by MICHAEL W. ROSS. New York: Haworth Press. 1988. 212 pp. $29.95.

Psychiatry, indeed society as a whole, divides into those who regard homosexuality as a pathology and those who regard it as a variant of normality. In recent years AIDS has brought this dilemma very much into focus. This book, published in America although with an Australian editor, represents the output of a growing number of psychotherapists and psychiatrists who regard homosexuality as a normal variation. The papers were originally published as two volumes of the *Journal of Homosexuality*, and many of the authors identify themselves with gay activist groups or groups of gay professionals.

The central message of the book is that the problem for the homosexual is not his sexual orientation but arises as a result of "society-wide process of stigmatisation that has negative social, economic, and emotional effects on its victims." The view is clearly expressed that, "the gay man or lesbian who is in psychotherapy may be at significant risk if they work with a psychotherapist who believes that homosexuality is an expression of abnormality or mental illness".

Given this basic point of view, what does the book achieve? Although many of the authors devote an excessive amount of space to proving that homosexuality should not be regarded as pathology (clearly the decisions in 1973 and 1980 by the American Psychiatric Association have not resolved the matter), it succeeds in giving a clear view of the problems of the homosexual as perceived by these therapists and presumably by a large number of the gay community. The perspective is psychosocial, not psychoanalytic. Psychotherapy is seen largely as helping the person to come to terms with his or her homosexuality, to regard it as normal, and to counteract the effects of homophobia.

The techniques advocated are supportive psychotherapy, counselling, and a mixture of behavioural approaches. Specific psychiatric disorders are seen as basically the same as those occurring in heterosexuals, but with the added problems of social isolation and stigmatisation. Clearly, the classical psychoanalytic approach is seen as antitherapeutic.

Two papers seem somewhat out of place. The first is a fascinating case study of a paedophilic murderer, and the second is a paper aiming to show that borderline personality disorder is a social dilemma resulting from the changing social norms of the 20th century. I am not really convinced by the arguments, nor by the excellent case history of a homosexual man which is used to substantiate it. One is, however, left wondering whether it does not undermine the central tenet of the book.

ROBERT HALE, *Consultant Psychotherapist, Tavistock Clinic, London*

Research, Comparisons and Medical Applications of Ericksonian Techniques. (Ericksonian Monographs. No. 4). Edited by STEPHEN R. LANKTON and JEFFREY K. ZEIG. New York: Brunner/Mazel. 1988. 130 pp. $34.00.

Here is yet more from the followers of the late Milton Erickson. The first four chapters of this slim volume report the results of research studies. Topics include the relative effectiveness of direct and indirect suggestions, the value of 'hypnotic-relaxation' cassettes in a gynaecologic-obstetric ward, and whether the capacity to undergo hypnosis is innate or learned.

The next two papers are theoretical discussions comparing Erickson's techniques with, respectively, cognitive therapies and redecision therapy. They argue that Erickson's methods had more in common with the other therapies than might appear at first sight.

The final three articles – on medical applications – are a mixed bag. That on the "application of Ericksonian principles to the use of medication" I found superficial and unsatisfactory. In one case, the prescription of alprazolam was continued for strategic therapeutic reasons related to the family dynamics. The dangers of prolonged administration of benzodiazepines were apparently not considered. Juliet Auer gives us some anecdotal, although quite interesting, accounts of how she uses techniques derived from Erickson's work in the renal unit of a hospital. Perhaps the best paper in this section is that by Bob Britchford, on the use of the 'ten-minute-trance' in general practice.

While there is material of interest here, it is difficult to see why it needed to be published in this rather expensive form. Most of the articles would probably have been accepted by one of the regular journals in the field, and the others did not need publishing at all. I expect that the libraries of hospitals and clinics in which hypnotherapists work, and some 'hardcore' Ericksonians, will want to buy the book. For others there is better value elsewhere in the Ericksonian literature.

PHILIP BARKER, *Professor of Psychiatry and Paediatrics, University of Calgary*

Going Somewhere: People with Mental Handicaps and their Pastoral Care. By SHEILA HOLLINS and MARGARET GRIMER. London: SPCK. 1988. 121 pp. £4.95.

Radical changes in patterns of care during the past two decades have both increased the overall numbers of mentally handicapped people in the community and also considerably raised their profile. This has left many people, both lay and professional, exposed to their own personal inadequacies of training and understanding in this area. Many who want to help will find a lack of suitable literature on the subject. This book, which was stimulated by a one day conference on pastoral care, helps to fill the gap. It provides answers in plain English to the common questions likely to arise in the minds of those who come new to the subject, setting out the basic facts clearly and sensitively, and advising on the everyday situations likely to be encountered, such as sexuality, personal relationships, bereavement, and dealing with parents. With its sensible straightforward approach it can confidently be recommended to a wide range of workers. Although specifically aimed at those outwith the mentally handicap services, many within will benefit from the perspective offered. My only criticism of this otherwise excellent little book is the rather uncritical embrace of the concept of community care which pervades the text. One wishes that the authors had found the space to point out and discuss some of its attendent problems.

KENNETH DAY, *Consultant Psychiatrist, Northgate Hospital, Morpeth, Northumberland*

Receptors and Ligands in Psychiatry. Edited by A. K. SEN and T. LEE. Cambridge: Cambridge University Press. 1988. 604 pp. £75.00.

The theme of this series on intercellular and intercellular communication is the analogy between cellular communication and language. The mechanism by which neurones communicate with one another is largely through chemical signals. This resembles a language, whose vocabularly is the interaction of individual neurotransmitters or neuromodulaters (the 'ligands') with neuronal membrane structures (the 'receptors'). Psychiatric disease can be analysed in terms of abnormalities in the vocabularly, leading to inappropriate messages and inappropriate responses.

The central neurotransmitters about which most is known are dopamine, noradrenaline, acetylcholine, and serotonin. The main pathways for neurones using these transmitters are now fairly well defined. Much more complicated is the variety of receptors for each of these transmitters, but this is gradually becoming elucidated. The development of new drugs that bind specifically to separate classes of each receptor (for instance DA1 and

DA2 receptors) should lead to new understanding of mental disorders, and their treatment and pathogenesis. More obscure and not really addressed in the volume is the way in which changes in one transmitter-receptor class affects other transmitters and receptors.

Here, 25 leading authorities review topics covering particular transmitters in relation to schizophrenia, affective disorders, anxiety, and stress. In addition to chapters on the transmitters mentioned above, here are others dealing with benzodiazepine receptors, the neuropeptides, CCK and neurotensin, and their ligands. There are also good reviews of endocrine studies of schizophrenia, of animal models of mental illness, and of the neuropathology of schizophrenia.

There is little mention of GABA and none of adenosine, both of which are likely to be important in the pathogenesis of anxiety, nor of glycine and the excitatory amino acids.

The volume is attractively printed, and the reviews are well written and as up to date as could be expected. It is a helpful source book for research workers in biological psychiatry.

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Psychotherapy and the Creative Patient. Edited by E. Mark Stern. New York: The Haworth Press. 1988. 174 pp. $24.95.

This is a multi-author American textbook, apparently part of a series on special types of patient. The authors are mainly psychologists. The chapters cover various aspects of therapeutic techniques, and empirical research is also reported. Although the book purports to be about the "creative patient", in fact it ends up being rather muddled between patients whose profession is in the arts, psychotherapy as a creative process, and the therapist's own creativity.

Some of the individual chapters are good. In particular, the account by Natchez of the lives and marriage of the Mexican artists Diego Rivera and Frida Kohl makes poignant and fascinating reading. Unfortunately, the weak chapters predominate. There is a report of research into hemispheric specialisation, from which broad generalisations are made. However, there is no mention in the discussion of the possible implications of the fact that most of the subjects were Catholic priests. The opening chapter consists of a dialogue between Mark (the editor) and Virginia Stern, on creativity. It is replete with indigestible jargon and grammatical errors. Worst of all is the chapter by Zaraleya-Harari. She describes a patient doing secretarial work for her, a patient who gave her daughter a bizarre name which incorporates the therapist's surname, and becoming involved in the patients' professional lives. This sort of work should not merit a place in a textbook on psychotherapy.

There is much that needs to be said about the ways in which therapy can foster creativity, about the creativity of the process itself, and about the pleasures and pitfalls of working with patients who have special talents. This book does not do justice to the subject, and cannot be recommended.

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New editions

Handbook of Clinical Psychopharmacology (2nd edn). Edited by J. P. Tupin, R. I. Shader and D. S. Harnet. Northvale, NJ: Jason Aronson. 1988. 486 pp.

This edition of the *Handbook* contains 17 chapters by 23 contributors, and it is an exceptional volume. Far from being unemotionally chemical, it emphasises a broad view of psychopharmacology, the importance of precision in clinical practice, and the practical and caring management of patients. In keeping, plenty of space is given to diagnosis and differential diagnosis. The use of drugs is described with a sense of precise application, expectation, and outcome. Limitations are not concealed, but in the light of recent general experience more could be included about what might be called the natural history of using benzodiazepine compounds and about the substances which can alter the effectiveness of antidepressants.

The style of each of the chapters is similar. They are organised clinically, space being allotted according to prevalence in practice. The early sections cover psychoses, depressive disorders, fear and anxiety, and mania. Modern classification is used and explained. The chapters which follow provide an answer for many of the present-day practical pharmacological problems of the clinic and acute ward. Violence is considered as a possible product of the use of drugs, and then the chemical management of violence is described. Substance abuse is fully covered, and among the range of special problems discussed are memory disturbance and cognitive impairment in the elderly, children's disorders, eating disorders, atypical depression, adult hyperactivity, and treatment resistance. Further detailed help is given in chapters devoted to drug combinations, the use of serum levels, and the combination of psychotherapy with psychopharmacology. The latter is introduced with intriguing skill. The quotation "the implication is that psychotherapy joins pharmacotherapy in the ranks of biological therapies" should be read in context, and gives an indication of the breadth of view of the work as a whole. The growing caution imposed by increasing negligence claims in the USA is placed in perspective in a sound penultimate chapter. This is followed by a short glossary of terms.

This is a substantial work, rich in essentials and unpretentious. The diagnostic detail is particularly well chosen, and it is provided to a degree often missing from work dedicated to physical treatment. It is essentially readable, and although the unavoidable frequent abbreviations have a jarring effect, the scale-pan type of review approach has been avoided and documentation, although perhaps over-selective in places, is adequate. There must be few works of this magnitude on this subject in which there are no printed chemical formulae, in which the 'caring' approach for patients is so apparent, and in which there is a good deal of plain clinical psychiatry of the 'hands on' sort, helpful for trainees.

The context, plan, and sentiment of the book is a powerful mixture, and quite apart from its instructive potential it is enjoyable to read.

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Reality Orientation: Psychological Approaches to the 'Confused' Elderly (2nd edn). By UNA P. HOLDEN and ROBERT T. WOODS. Edinburgh: Churchill Livingstone. 1988. 353 pp. £11.95.

This is an excellent book and an enjoyable read. The preface to this edition suggests that the "book was never intended to be just about reality orientation", and the authors cover a wide range of psychological topics from basic behavioural programmes for incontinence to advanced reality orientation (RO) groups. The book is divided into two parts: the first, 'Theory and research', is well balanced by the second, 'Practical application', which includes 101 ideas for formal RO sessions and discusses theoretical and practical issues in different settings, from an ill-designed hospital ward to the patient's home. There is a welcome emphasis throughout on staff attitudes, and their positive approach is very encouraging to those of us who agree that "attitudes towards the elderly in western society have often in the past been discriminatory, rejecting, and negative".

The book is written by psychologists, but is accessible to all disciplines, and the particularly useful chapter on 'The basic approach – RO in everyday use' should be compulsory reading for all involved in the care of demented patients. It is essentially guidance about how to approach and converse with confused people on a day-to-day basis. It broadens the concept of RO from a specific treatment to a sensitive, individualised, non-threatening approach to the confused patient to be used in every interaction. There is a good chapter on assessment, stressing the usefulness of and the amount of information which can be obtained from informal testing, using everyday objects and interactions, e.g. looking at a magazine, rather than subjecting the patient to the greater anxiety of a formal testing situation. The book is informative about RO, and contains a list of references from a wide variety of sources, but its special contribution to the field is its emphasis on attitudes regardless of which psychological approach is used.

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Human Ageing. An Introduction to Gerontology (3rd edn). By D. P. BROMLEY. Harmondsworth: Penguin. 325 pp. £5.95.

This is the third edition of a book with an established pedigree, and provides a precise and clear introduction to the psychology of human ageing, and more. It differs from the second edition in that the section on the history of human ageing has been removed, and much more emphasis is placed on the interrelation of the various facets that make up the study of gerontology. This is well demonstrated by the introduction of a new section on social policy and the elderly, which examines in depth the political and social pressures which can be brought to bear by the elderly and also the difficulties experienced by elderly people subjected to social prejudice in terms of welfare provision.

The section on psychological disorders is a bit thin, and the terminology used a little outdated, but this is not specifically a textbook of psychiatry and is designed for a much wider readership. If anything, the book suffers from having too much information in one text, and is certainly too concentrated to read comfortably in a single sitting. Nonetheless, it does provide a broad information base and should be considered a valuable addition to any library, from the local library to the specialist psychiatric library. At £5.95 it is very good value for money.

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Annotation

Foetal Learning:
Implications for Psychiatry?

PETER G. HEPPER

> "The history of man for the nine months preceeding his birth would, probably, be far more interesting and contain events of greater moment than for all the three score and ten years that follow it." Samuel Taylor Coleridge (1885)

The idea that the individual is affected by experiences in the womb has been present in various forms since the beginning of science. For example, Aristotle in *De Generatione Animalium* speculates that it is during pregnancy that sensation is first acquired. This idea persisted through medieval society and was acknowledged by Locke in his *Essay Concerning Human Understanding* (1690), in which he argued that the foetus may be capable of forming some ideas. Of course such views were opposed by others, for example Rousseau, who viewed the foetus as a witless tadpole.

It was only in the early 20th century that researchers directly addressed the question of foetal behaviour and in particular foetal learning. Perhaps the first experimental study to demonstrate foetal learning was performed by Peiper (1925). Peiper was interested in the foetus's response to noise, and during the late stages of pregnancy sounded a 'loud and shrill' motor-car horn within a few feet of the mother's abdomen. He noted that this elicited marked movements in the foetus. More interestingly, he found that repetition of the noise elicited no response. From this he deduced that the foetus is able to hear sounds within the womb. While it would be easy to criticise this study on methodological grounds, it does represent the first demonstration of learning, i.e. habituation, in the foetus, and, it should be noted, has been replicated using the most modern technology and methodology (e.g. Madison *et al*, 1986). Peiper's paper represents a landmark in the study of the behavioural capabilities of the foetus for, as Peiper states, "Knowledge of this ability is important, for up to this time the foetus has been denied any form of thought process or consciousness".

Since this early study, reports of foetal learning have been sporadic. This has partly been due to a lack of technology with which to observe and monitor the foetus, but it is also due to the prevailing views held concerning the capabilities of the newborn. Since the newborn was considered to have little capacity to respond and behave, why study the foetus, which would have even less? However, as experiments revealed how competent the newborn is, and as technology, in particular ultrasound scanning, became more advanced and available, the last ten years have seen renewed and sustained interest in foetal behaviour and in particular foetal learning.

The study of foetal learning can be broadly divided into two areas, based upon when evidence of learning has been sought. Thus some have attempted experimentally to condition the foetus and observe the effects of such conditioning in the womb, while others have observed the effects of 'normal' foetal experience or conditioning in the newborn.

First, studies which have observed conditioning in the womb are considered. Ray (1932) made the first attempt to classically condition the foetus. Vibration was used as the conditioned stimulus (CS) and this was paired with a loud bang as the unconditioned stimulus (UCS). No data are reported as to the success of conditioning, although, in the last line of the paper, it is reported that the newborn suffered "no ill effects from her prenatal education". Spelt (1948) repeated the experiment, again using vibration as the CS and a loud sound as the UCS. He reported successful conditioning for foetuses in the last two months of pregnancy, such that after 15–20 pairings the conditioned stimulus alone elicited movement. Feijoo (1975, 1981) attempted to condition the foetus with music as the CS, paired with relaxation of the mother as the UCS. After 24 pairings, foetuses aged 30–37 weeks stopped moving on hearing the music. Furthermore, the effects of conditioning were retained after birth for those foetuses who had been conditioned between 22 and 36 weeks of age. Six minutes after birth conditioned babies stopped crying, opened their eyes, and showed fewer clonic movements on hearing the music. I have found no reports of instrumental conditioning in the foetus.

By far the most popular technique for observing conditioning *in utero* is that of habituation, whereby repeated stimulation, usually vibration, causes a decrease in response (Thompson & Spencer, 1966). Habituation of body movements (Sontag & Wallace, 1934; Leader *et al*, 1982*a*) and heart rate response (Goodlin & Lowe, 1974; Granier-Deferre *et al*, 1985) have been observed. Habituation has been demonstrated as early as 23 weeks of gestational age and appears first in females (Leader *et al*, 1984). Of particular note is the study by Madison *et al* (1986) which, following guidelines set by Jeffrey & Cohen (1971) for the observation of true habituation and not adaptation, found that foetuses aged 28–37 weeks did truly habituate to a vibrational stimulus.

Other researchers have observed the newborn's response to stimuli experienced in the womb in order to show foetal conditioning. Salk (1960, 1962) demonstrated that the newborn responded to the sound of a heartbeat of 72 beats per minute (normal maternal heartbeat) but became restless on exposure to one of 128 b.p.m. He found that newborns who heard the heartbeat put on more weight and cried less than controls who did not hear it. Furthermore, infants aged 16–37 months fell asleep faster if played the sound of a heartbeat at 72 b.p.m. at bedtime than those played no sound, a metronome at 72 b.p.m., or a lullaby. This stimulated much research examining the effects of heartbeat as a stimulus and produced a market in tapes of maternal heartbeat for parents of children who were reluctant to sleep. The effects of heartbeat have not always been supported, especially outside the immediate neonatal period, and many studies have methodological flaws (see Detterman, 1978, for review). More recently, it has been demonstrated that heartbeat is reinforcing for newborns, as babies will alter their sucking pattern to obtain more of the heartbeat sound (DeCasper & Sigafoos, 1983). Salk (1960) claimed the foetus learned about the maternal heartbeat while in the womb, either by a process of "imprinting" or by association with the "tension free state of the foetal nervous system". While the sound of the mother's heartbeat may be experienced in the womb (although see Armitage *et al*, 1980) it remains to be determined whether the neonate learns about it during its time in the womb or whether the effects are the result of a genetically determined response to resting adult heartbeat.

Others have examined the response of neonates to voices, in particular that of their mother. The possibility of the foetus hearing voices in the womb has long been acknowledged ("For behold, when the voice of your greeting came to my ears, the babe in my womb leaped for joy" (Luke 1:44)). DeCasper & Fifer (1980) examined the ability of newborns under three days of age to alter their sucking pattern to receive the voice of their mother. Newborns were observed sucking for a baseline period in which the median interval between sucks was obtained. Individuals were then given the opportunity to hear their mother's voice by increasing the time between sucks or the voice of another female by decreasing the time between sucks, or vice versa. Newborns altered their sucking to hear their mother's voice. Interestingly, however, in a similar task, newborns did not alter their sucking pattern when given a choice of their father's or another male's voice (DeCasper & Prescott, 1984). These studies, as well as demonstrating sophisticated learning capabilities in the newborn, indicated the possibility of pre-natal influences on post-natal preferences for voice. The question of pre-natal experience was addressed directly in a later study in which mothers read a particular passage to their foetus during pregnancy (DeCasper & Spence, 1986). Newborns after birth were tested as above and given a choice between the story read to them by their mother during pregnancy but here recited by other women and a novel story, never heard before, read by the same women. Newborns altered their sucking to receive the story they had been read by their mother during pregnancy, even though during the experiment it was read by other women. This study indicates that the foetus has learned and remembered something about the acoustic cues that specified the story read to them in the womb, and conclusively demonstrates pre-natal learning of acoustic cues in the womb.

Most recently, I examined the response of newborns to the tune of their mother's favourite television soap opera (Hepper, 1988). It was found that on hearing the theme tune, in this case that of "Neighbours" (BBC1), the infants of mothers who watched the programme stopped crying and became alert, whereas infants of mothers who did not watch it showed no reaction. It thus appears that the ubiquitous soap operas pervade even the womb.

This review indicates that there can now be little doubt that the foetus can learn in the womb. At first glance it may appear that the ability of the foetus to learn has little implication for psychiatry. However, first impressions are misleading. The psychoanalytic tradition has acknowledged that events *in utero* or during birth can affect later behaviour, emotions, and attitudes, and techniques of regression to the pre-natal period, or 'rebirthing', have been used to overcome a variety of disorders (see Fedor-Freybergh & Vogel, 1988), although whether any such regression takes place is open to question. Indeed, at the Institute of Advanced Studies in California one can partake of a class on "Healing Your Prenatal Memories" which enables people to explore and heal their pre-natal and birth memories. Lake argued that it was during the first trimester that the origins of disorders such as depression, anxiety, phobias, paranoia, and schizophrenia could be found (Ridgway, 1981). The idea of mental health being influenced by uterine events is certainly not new. As early as the 5th century BC, Caraka, an early Indian embryologist, was writing about a variety of psychological factors that may cause mental imbalance in the foetus (Gupta & Datta, 1988). Holt (1931) acknowledged that intrauterine conditioning may account for certain behavioural characteristics of the neonate. Foetal learning may indeed have implications for psychiatric disorders. I should like to consider three areas, diagnosis, aetiology, and treatment, where the ability of the foetus to learn may be of relevance.

Diagnosis

As indicated above, the idea of disorders originating during the foetal period is well established (although it should be noted that hard evidence to this effect is lacking). It therefore follows that it might be possible to diagnose these during this period. Similarly, for disorders that have a genetic component, indicators may be present during the foetal period that enable the disorder to be identified. At a very general level, the ability to learn implies that the foetus has a certain level of sensory competence, associative and memory capabilities. Assessment of foetal learning may be used to discover deficiencies in these abilities which in turn may be indicators of disorders in later life. For example, inability to learn during the foetal period may be indicative of some mental retardation or learning disability.

For any tests of foetal learning to be used as a diagnostic tool requires substantive information regarding the 'normal' population's abilities for learning, as well as correlations between pre-natal deficiencies in learning and post-natal outcome. We are a very long way from this. However, one technique which looks promising and may well be utilised in the future is that of habituation. Post-natally, deficits in habituation have been reported in hyperactive children (Hutt & Hutt, 1964), Down's syndrome (Dustman & Callner, 1979), and schizophrenics (Gruzelier & Venables, 1972). More recently, performance on habituation tasks during the first year of life has been found to be predictive of later cognitive functioning (Rose & Wallace, 1985; Bornstein & Sigman, 1986). Preliminary studies of the foetus have indicated habituation deficits in microcephalic and anencephalic individuals (Leader *et al*, 1982*b*). Habituation may, therefore, be used in the early diagnosis of later disorders. While the ability of this technique to predict specific disorders is unknown, it may enable the early identification of 'at-risk' individuals and perhaps enable corrective measures to be undertaken.

Treatment

If it is possible to diagnose disorders pre-natally then, theoretically, it would be possible to instigate treatment of the disorder during this period. If the conditions under which specific disorders arise could be determined, it should be possible to arrange contingencies to overcome this and thereby prevent the disorder. Below, however, I consider the possibility of treatment at the level of general stimulation of the foetus rather than specific intervention programmes for specific disorders.

The possibility of stimulating the foetus was encompassed in the Talmudic writings of 2nd–6th-century Jews, and therefore, cannot be considered as new. Recent years have seen much interest in the effects of early stimulation on later achievement, or 'hot-housing'. A general conclusion from these studies is that stimulation can increase abilities although not to the extent of producing geniuses (Howe, 1988). Certainly, for a variety of conditions, including Down's syndrome, stimulation can increase a child's capabilities.

Given that stimulation can have beneficial effects post-natally, it should be considered whether pre-natal stimulation could similarly benefit those 'at risk', or for that matter the 'normal' foetus. Programmes of foetal stimulation are relatively new, and experimentally evidence is lacking, although there is a suggestion that pre-natal stimulation enhances the newborn's physical development and maturation (Van de Carr *et al*, 1988). However, appropriate controls, especially for the effects of general increased interest in the pregnancy, were not conducted so it is difficult to attribute the effects to pre-natal stimulation alone. In America, a 'Pre-Natal University' has been established, at which pregnant mothers interact with their foetus (Walmsley & Margolis, 1987). It is reported that 'graduates' show greater physical and mental development than newborns who had not attended the 'University'. Again, good, controlled, evidence is sparse regarding the effectiveness of such stimulation. The possibility does exist that stimulation may help the 'at-risk' foetus, but much more research is required.

Aetiology

The idea of the pre-natal period contributing to later psychiatric disorder is not new, although the role of learning in such disorders has received scant attention. Since the foetus can learn and retains this memory after birth (but see below), foetal learning may be implicated in the aetiology of certain psychiatric disorders. Theoretically, as well as being positively conditioned in the womb, the human foetus could also be aversively conditioned. This has been demonstrated in animals (e.g. by Smotherman, 1982), and there is little reason to suspect it would not be the case in humans. One problem facing researchers is in determining the duration of foetal learning. Studies of heartbeat, maternal voice, and television theme tunes face problems because the individual experiences these stimuli after birth and thus it is difficult to determine the duration of any pre-natal learning, since the individual will have encountered these stimuli post-natally. Certainly, under hypnosis people of all ages have been reported to remember experiences from the womb (Verny, 1981). The duration of pre-natal learning and its effectiveness in later life have yet to be determined. It may be that foetal learning is the first stage of a descending spiral leading to disorder. Behaviour acquired in the womb would predispose the individual to respond in certain ways after birth. These would further reinforce inappropriate actions, and the cycle might continue and develop into a psychiatric disorder.

One learning paradigm that may be particularly relevant is that of learned helplessness. This procedure involves exposing the subject to unsignalled, inescapable shocks (usually electric), over which the individual has no control. Experience of learned helpelessness results in interference in the acquisition of behavioural skills and has been implicated as a factor in the aetiology of depression (e.g. Hellhammer, 1983). While not exactly comparable to the situation outside the womb, the situation of the foetus is similar in some aspects to the laboratory animals undergoing such experiments. The foetus has little control over the stimulation it receives and it is unable to escape from it. A number of stimuli may be aversive, for example, loud noises, nicotine, or, perhaps most interestingly, stress. The foetus responds to maternal emotions, including stress, reactions which may be mediated by substances (e.g. hormones, catecholamines) crossing the placenta, by increased maternal arterial pressure, or by increased maternal muscle tone reducing the available space for movement in the womb. Whether these are aversive to the foetus is unknown, but certainly such stimulation is unsignalled, inescapable, and uncontrollable. It may be that the foetuses of highly stressed mothers experience a situation very similar to that of animals in learned helplessness experiments. Such experiences may contribute specifically to the onset of particular disorders, for example, depression, or, perhaps most likely, will predispose the individual to respond in certain ways that increase the likelihood of suffering from psychiatric disorder in later life.

One line of very recent research which may be of relevance here is in the field of psychoneuroimmunology (see Ader, 1981), where evidence suggests the immune system may be conditioned. Under conditions of helplessness, cortisol is released which depresses the functioning of the immune system. It is interesting to speculate that stimuli could become conditioned in the womb which depress the immune system. In later life experience of such stimuli result in depression of the immune system, and this may be a causal factor in certain psychosomatic illnesses, where psychological factors induce 'illness'.

At a more general level, the fact that pre-natal experiences can affect post-natal behaviour means we must reassess the pre-natal period. Although our present knowledge of foetal behaviour and experience is small, the evidence does not suggest that experiences during the pre-natal period are important formative influences on later life. Whether such experiences exert specific effects on behaviour or act more generally to predispose the individual's behaviour in certain ways has yet to be determined, but one thing is certain – the pre-natal period cannot be overlooked.

Summary

While many of the ideas presented concerning foetal learning and their implications for psychiatry are at present speculative, I would remind people of the words of Carmichael (1954):

> "a study of adult behaviour without consideration of its origin before birth is as incomplete as . . . the study of adult anatomy without reference to the embryology of the structures considered."

It is folly to overlook the foetal period!

References

Ader, R. (ed.) (1981) *Psychoneurolmmunology*. New York: Academic.

Armitage, S. E., Baldwin, B. A. & Vince, M. A. (1980) The fetal sound environment of sheep. *Science*, **208**, 1173–1174.

Bornstein, M. H. & Sigman, M. D. (1986) Continuity in mental development from infancy. *Child Development*, **57**, 251–274.

Carmichael, L. (1954) The onset and early development of behavior. In *Manual of Child Psychology* (2nd edn) (ed. L. Carmichael), pp. 60–185. New York: J. Wiley.

DeCasper, A. J. & Fifer, W. P. (1980) Of human bonding: newborns prefer their mothers' voices. *Science*, **208**, 1174–1176.

—— & Sigafoos, A. D. (1983) The intrauterine heartbeat: a potent reinforcer for neonates. *Infant Behavior and Development*, **6**, 19–25.

—— & Prescott, P. A. (1984) Human newborns' perception of male voices: preference, discrimination and reinforcing value. *Developmental Psychobiology*, **17**, 481–491.

—— & Spence, M. J. (1986) Prenatal maternal speech influences newborns' perception of speech sound. *Infant Behavior and Development*, **9**, 133–150.

Detterman, D. K. (1978) The effect of heartbeat on neonatal crying. *Infant Behavior and Development*, **1**, 36–48.

Dustman, R. E. & Callner, D. A. (1979) Cortical evoked response and response decrement in non-retarded and Down's syndrome individuals. *American Journal of Mental Deficiency*, **83**, 391–397.

Fedor-Freybergh, P. & Vogel, M. L. V. (1988) *Prenatal and Perinatal Psychology and Medicine*. Carnforth, Lancs: Parthenon.

Feijoo, J. (1975) Ut conscientia Noscatue. *Cahier de Sophrologie*, **13**, 14–20.

—— (1981) Le foetus Pierre et le loup . . .ou une approche originale de l'audition prenatale humaine. In *L'aube des Sens* (ed. E. Herbinet & M. C. Busnel). Paris: Stock.

Goodlin, R. C. & Lowe, E. W. (1974) Multiphasic foetal monitoring. A preliminary evaluation. *American Journal of Obstetrics and Gynecology*, **119**, 341–357.

Granier-Deferre, C., Lecanuet, J. P., Cohen, H., *et al* (1985) Feasibility of prenatal hearing test. *Acta Otolaryngol (Stockholm)* (suppl. 421), 93–101.

Gruzelier, J. H. & Venables, P. H. (1972) Skin conductance orienting activity in a heterogenous sample of schizophrenics. *Journal of Nervous and Mental Disorders*, **155**, 277–287.

Gupta, D. & Datta, B. (1988) The cultural and historical evolution of medical and psychological ideas concerning conception and embryo development. In *Prenatal and Perinatal Psychology and Medicine* (eds P. Fedor-Freybergh & M. L. V. Vogel), pp. 507–534. Carnforth, Lancs: Parthenon.

Hellhammer, D. (1983) Learned helplessness – an animal model revisited. In *The Origins of Depression: Current Concepts and Approaches* (ed. J. Angst), pp. 147-162. Berlin: Springer-Verlag.

Hepper, P. G. (1988) Foetal 'soap' addiction. *Lancet*, *I*, 1347-1348.

Holt, E. B. (1931) *Animal Drive and the Learning Process*. London: Williams & Norgate.

Howe, M. J. A. (1988) "Hot-house" children. *Psychologist*, **1**, 356–358.

Hutt, S. J. & Hutt, C. (1964) Hyperactivity in a group of epileptic (and some non-epileptic) brain damaged children. *Epilepsia*, **5**, 334–351.

Jeffrey, W. E. & Cohen, L. B. (1971) Habituation in the human infant. *Advances in Child Development and Behavior*, **6**, 63–77.

Leader, L. R., Baillie, P., Martin, B., *et al* (1982*a*) The assessment and significance of habituation to a repeated stimulus by the human foetus. *Early Human Development*, **7**, 211–219.

——, ——, ——, *et al* (1982*b*) Foetal habituation in high risk pregnancies. *British Journal of Obstetrics and Gynaecology*, **89**,441–446.

——, ——, ——, *et al* (1984) Foetal responses to vibrotactile stimulation. A possible predictor of foetal and neonatal outcome. *Australian and New Zealand Journal of Obstetrics and Gynaecology*, **24**, 251–256.

Madison, L. S., Adubato, S. A. Madison, J. K., *et al* (1986) Foetal response decrement: true habituation. *Developmental and Behavioral Pediatrics*, **7**, 14–20.

Peiper, A. (1925) Sinnesemp findungen des Kindes vor seiner geburt. *Monatsschrift für Kinderheilkunde*, **29**, 237–241.

Ray, W. S. (1932) A preliminary report on a study of foetal conditioning. *Child Development*, **3**, 175–177.

Ridgway, R. (1981) Foetal memory: fact or fiction? *BMA News Review*, April, 13–18.

Rose, S. A. & Wallace, I. F. (1985) Visual recognition memory: a predictor of later cognitive functioning in preterms. *Child Development*, **56**, 843–852.

Salk, L. (1960) The effects of the normal heartbeat sound on the behaviour of the new-born infant. Implications for mental health. *World Mental Health*, **12**, 168–175.

—— (1962) Mothers' heartbeat as an imprinting stimulus. *Transactions of the New York Academy of Science*. **24**, 753–763.

Smotherham, W. P. (1982) Odor aversion learning by the rat foetus. *Physiology and Behavior*, **29**, 769–771.

Sontag, L. W. & Wallace, R. F. (1934) Preliminary report of the Fels Fund. Study of foetal activity. *American Journal of Diseases of Children*, **48**, 1050–1057.

Spelt, D. K. (1948) The conditioning of the human foetus *in utero*. Journal of Experimental Psychology, **38**, 338–346.

Thompson, R. F. & Spencer, W. A. (1966) Habituation: a model for the study of neuronal substrates of behavior. *Psychological Review*, **73**, 16–43.

Van de Carr, K., Van de Carr, R. & Lehrer, M. (1988) Effects of prenatal intervention program. In *Prenatal and Perinatal Psychology and Medicine* (eds P. Fedor-Freybergh & M. L. V. Vogel), pp. 489–496. Carnforth, Lancs: Parthenon.

Verny, T. (1981) *The Secret Life of the Unborn Child*. New York: Summit.

Walmsley, J. & Margolis, J. (1987) *Hot House People*. London: Pan.

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Review Article

The Genetics of Depression and Manic–Depressive Disorder

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Depressive disorders are more common in the relatives of depressed probands than in the population at large, and there is compelling evidence that the familial aggregation of bipolar disorder and severe unipolar depression is at least partly due to genetic factors. However, the evidence concerning 'non-endogenous' depression is less clear, and family environment probably plays a stronger role. Much current research is focused on two areas: firstly, the mode of inheritance of manic-depressive illness, with the use of molecular biological techniques to detect and localise major genes; and secondly, the ways in which familial predisposition and environmental insults combine to produce depressive disorder.

Defining the phenotypes

Depression is among the most ubiquitous of psychiatric symptoms. Indeed, it has been estimated, on the basis of a study in an inner-London suburb, that seven out of ten women and more than four out of ten men will have had at least one clinically significant depressive episode by the age of 65 years (Bebbington *et al*, 1989). Of course, much depends on the definition of 'a case' and what is to be regarded as clinically significant, so that there are inevitably large variations in estimates of the prevalence of depression (Eastwood & Kramer, 1981). Faced with these facts, investigation of the role of genes in affective disturbance is daunting, for we must deal with a phenotype which is common, ambiguous, and elastic. Nevertheless, the observation that the condition tends to cluster in families provides one of the most constant aetiological clues about depression.

The most straightforward manoeuvre is simply to ignore diagnostic subtlety and nuance, and restrict consideration purely to more severe affective disorders. Thus, for the first part of this review, we assume in our survey of genetic studies that it is possible to define a severe, less common category of typical clinical depression that is qualitatively quite distinct from milder, commoner forms.

Family studies

Early studies which adopted a narrow Kraepelinian definition of manic–depressive illness consistently found that the disorder was more common in the relatives of index cases than in the general population (Slater & Cowie, 1971). However, over the past two decades, it has become the rule in family studies to avoid lumping all manic–depressive illness together and instead to divide it into unipolar (UP) disorder, in which there are attacks only of depression, and bipolar (BP) disorder, in which there are episodes of both mania and depression (or less commonly of mania alone). This distinction, originally due to Leonhard (1959), was employed by Angst (1966) in Switzerland and Perris (1966) in Sweden, working independently. Perris found a quite striking degree of homotypia, that is a tendency for UP and BP disorder to 'breed true', with secondary cases among relatives conforming to the same pattern of illness as was found in index cases. The pattern uncovered by Angst (1966) was more complex. There was an apparent increase only of UP disorder in the relatives of UP probands. Among the relatives of BP probands an excess both of BP disorder and UP disorder was found. Most subsequent studies have found a similar pattern.

Previously, we have reviewed 12 studies of the relatives of BP probands and seven studies of the relatives of UP probands (McGuffin & Katz, 1986) (see Table I for summary). Table I shows a very large variation across studies, so that the morbid risk of affective disorder in the first-degree relatives of affectively ill probands ranges from 6% to 40%. It seems highly likely that the marked variation can be accounted for by differing diagnostic practices, but it may also be that there are true differences in the lifetime risk of affective illness in different populations. An intriguing and associated problem is that, in addition to geographical variation, there may be variation in prevalence rates of depression over time. It has been reported (Klerman *et al*, 1985) that there is a clear secular change in North America, with increases in the lifetime prevalence of major affective disorder among young cohorts. What is less clear is the explanation for this finding. While some believe it is a 'real' change, its magnitude would be difficult to explain on any genetic grounds and alternative explanations deserve serious consideration. For example, there may be an increased willingness of

TABLE I
Affective illness in the first-degree relatives of unipolar (UP) and bipolar (BP) probands (data from Studies reviewed by McGuffin & Katz, 1986)

Proband type	*No. of studies*	*Relatives*		
		Age-corrected[2] n *at risk*	*Morbid risk*[1] *(range): %* BP	UP
BP	12	3710	7.8 (1.5–17.9)	–
		3648	–	11.4 (0.5–22.4)
UP	7	2319	0.6 (0.3–2.1)	9.1 (5.9–18.4)

1. Weighted means.
2. Corrected denominator ('Bezugsiffer') to allow for relatives who have not lived through the period of risk.

younger subjects to volunteer depressive symptoms and an increased tendency of older groups to forget them (Bebbington *et al*, 1989).

The weighted average of morbid risks shown in Table I have to be compared with lifetime risks in the general population of about 3% for UP disorder and under 1% for BP disorder (Reich *et al*, 1982). Thus both forms of disorder appear to be strongly familial, but the average risk is greater in the first-degree relatives of BP probands, at about 19%, than in the relatives of UP probands, where it is just under 10%. A stronger familial effect in BP disorder is found in most but not all studies. Two investigations in the United States in which modern operational definitions of affective illness were employed found no substantial difference in the rates of disorder among the relatives of BP and UP probands (Tsuang *et al*, 1980; Rice *et al*, 1987). Why this was so is uncertain. The very large numbers involved in the study of Rice *et al* (1987) make sampling error an unlikely explanation, but the method of relying on a lifetime interview and inclusion of subjects in the BP category who give retrospective accounts of untreated mania (so-called bipolar-II disorder) may provide a more lax definition than is traditional.

Finally, it is important to note that although 'loaded' pedigrees are occasionally encountered that appear to have a dominant pattern of transmission, a broader survey of families compels the view that we are not dealing with a simple Mendelian disease. It is possible, even likely, that cultural factors contribute to the transmission of depression, and so it is essential to resort to twin and adoption studies, the classic methods of distinguishing genetic and environmental causes of familial clustering.

Twin studies

One immediate advantage of twin studies is that if we are merely attempting to assess whether genetic influences are present there is no necessary recourse to population figures. Thus a significantly higher concordance rate in monozygotic (MZ) than in dizygotic (DZ) twins is in itself persuasive evidence. Table II summarises three published sets of results and presents preliminary findings from our own study. The data are consistent in showing MZ concordance rates two to five times as great as DZ concordance rates and hence strongly suggest that genetic factors are important. The figures provided by Gershon *et al* (1975) represent a compilation of several older studies where the authors did not differentiate between UP and BP disorder. However, the study of Bertelsen *et al* (1977), based on Danish twin and psychiatric registers, did distinguish between the subtypes and found a considerable tendency to homotypia to occur. Thus 15 of the 19 affected identical cotwins of UP probands had UP disorder, while 21 of 27 identical cotwins of BP probands had BP disorder. However, these results should not be taken to indicate that UP and BP disorder are genetically distinct. Even allowing for diagnostic error and the possibility of later 'switches' in UP subjects to become BP, we cannot discount the fact that 10 out of 46 affected cotwins had a different form of affective illness from their respective probands.

The Danish twin study, like the majority of the family studies, suggests that BP disorder receives a stronger genetic contribution than UP disorder if we take as a rough guide the MZ:DZ concordance ratio. The concordance in MZ twins was 69% versus 19% in DZ twins when the proband had BP disorder (a ratio of 3.5:1). When the proband had UP disorder

TABLE II
Twin concordance for major affective disorder

Authors	n	*MZ Concordance %*	n	*DZ Concordance %*
Gershon *et al* (1975)[1]	91	69	226	13
Bertelsen *et al* (1977)[2]	69	67	54	20
Torgersen *et al* (1986)[2]	37	51	65	20
McGuffin & Katz (preliminary results)[2]	62	53	79	28

MZ, monozygotic; DZ, dizygotic.
1. Combined figures from six earlier studies reporting pair-wise concordance.
2. Systematic register-based studies reporting probandwise concordance.

the MZ concordance of 54% and DZ concordance of 24% gave a ratio of 2:1. The Norwegian study of Torgersen (1986), like that of Bertelsen *et al* (1977) and our own recent study, was based on a systematic sample obtained via a register. Torgersen set out to study moderately severe depression and therefore included only ten bipolar probands. This is likely to account for his lower overall MZ/DZ differences. Tending to confirm this view, we note that all four of the MZ cotwins of BP probands were affectively ill compared with none of the six DZ cotwins in Torgersen's small subsample. Our own study has focused on unipolar disorder and the preliminary findings given in Table II are based on a consecutive series of probands on the Maudsley Twin Register who fulfil DSM-III criteria for major affective disorder (American Psychiatric Association, 1980). The probands include a substantial number who received only out-patient treatment and so it is not perhaps surprising that results resemble those of Torgersen (1986) in his study of moderately severe depression.

The study of identical twins reared apart capitalises on a much rarer 'natural experiment'. The superficial appeal is great but the numbers involved are inevitably small and the data need to be interpreted with great caution because of potential sampling biases. Price (1968) and Farber (1981) have surveyed the world literature on reared-apart MZ twins which tends to support the classic twin study findings. Price reviewed reports of 12 reared-apart MZ twins where at least one had affective illness. Eight of these proved to be concordant giving, at 67%, a rate close to that for MZ twins reared together.

Adoption studies

Adoption strategies have been exploited much less extensively in studies of manic–depressive illness than in those of schizophrenia. The reason for this is not entirely clear, but we suspect that it relates to the fact that genetic research in affective disorder seems rarely to have provoked controversy or to have inflamed even the most partisan environmentalist.

A study with small numbers but with persuasive results (Mendlewicz & Rainer, 1977) showed that among the parents of 29 adoptees with BP illness, a significant increase in affective illness was found in biological compared with adoptive parents (28% v. 12%). Moreover, the rate of affective illness in the biological parents of adoptees did not differ significantly from that in the parents of bipolar non-adoptees (26%). It was also noteworthy that the majority of affectively ill biological parents had UP rather than BP disorder, once again suggesting that the two subtypes of disorder are unlikely to be distinct entities. A smaller and less complete investigation dealt mainly with UP illness but also found a significantly higher rate of affective disorder in adopted offspring of patients with affective illness than in adoptees whose natural parents were psychiatrically well (Cadoret, 1978). A Swedish study based mainly on health insurance records essentially studied four groups, the biological and adoptive parents of adoptees with affective illness, and the parents of matched control adoptees (Von Knorring *et al*, 1983). Surprisingly, no significant difference in the rates of affective illness were found between any of the groups, something which is difficult to explain on either genetic or environmental grounds. Subsequently, a study from Denmark found quite striking evidence of a genetic contribution to affective illness. Diagnoses were based on blind assessment of hospital records and showed an eightfold increase in UP depression and a 15-fold increase in suicide among the biological relatives of adoptees with affective illness compared with adoptive relatives and the relatives of matched control adoptees (Wender *et al*, 1986).

Therefore, despite certain inadequacies, the adoption data taken together with the family and twin evidence provide a compelling case in favour of an important genetic influence in the transmission of severe affective illness. We next have to ask what is transmitted and how is it transmitted?

Mode of inheritance and the search for major genes

What is inherited in severe affective illness is not the certainty of becoming ill but rather a liability to develop the disorder. Indeed, liability/threshold models provide us with the best conceptual framework for understanding the transmission of these and other common diseases that do not show simple Mendelian patterns of segregation. It is assumed that a variable termed 'liability to develop the disorder' is continuously distributed in the population such that only those whose liability at some time exceeds a certain threshold manifest the disorder. Stated in this way, the concept of liability threshold is perfectly general. Liability may be contributed to by genes, environment, or both. The simplest genetic hypothesis is that a single major locus (SML) is the only source of resemblance between relatives (James, 1971; Reich *et al*, 1972). Alternatively, we can postulate that genetic influences are mainly polygenic, that is, there are many genes at different loci contributing in a mainly additive way to liability. An additional source of family resemblance would be common environment. Again, if environment consists of multiple additive effects we would have a multifactorial (MF) continuum of liability in the population which would tend to be normally distributed (Falconer, 1965, 1981). However, in addition to SML and MF models a third possibility exists, the so-called mixed model. Thus, it is feasible to speculate that there is a major locus (or perhaps a number of different major loci) which shows its effects against a polygenic or multifactorial background (Morton & Maclean, 1974; Morton, 1982).

As we might expect in affective illness, the search for major gene effects has been focused on the more severe or 'more genetic' end of the spectrum of affective disorders. One study found that a combined or mixed model (major autosomal gene against a multifactorial background) provided a satisfactory explanation of the transmission of affective illness in a large sample of families ascertained through BP probands (O'Rourke *et al*, 1983). Similarly, an even larger sample of families, analysed by Rice *et al* (1987) using a mixed model approach, gave evidence for the presence of a major locus when controlling for the effects of birth cohort and age of onset. However, this evidence appeared less convincing when the mixed model was compared with a more general vertical transmission model (Lalouel *et al*, 1983). Thus when the probabilities of transmission of the major gene were not constrained to Mendelian values the likelihood increased significantly.

Family linkage studies using genetic markers provide a potentially more definitive and convincing means of demonstrating and localising major genes. Linkage studies have been reviewed by McGuffin (1988). The essential principle is that the co-segregation of a marker trait and a disease is studied. Within a pedigree, where a marker locus and a disease locus are in close proximity on the same chromosome, there will be a tendency for a particular marker allele to appear with the disorder. If, on the other hand, the marker and disease loci are far apart, independent assortment will occur. For example, if we study a disease transmitted via a single locus with two alleles *G* and *g*, and an unlinked marker locus at which there are two alleles *T* and *t*, then, on average, half the affected members of the family will have *T* and half will have *t*. If, on the other hand, the 'disease gene' *G* and the marker allele *T* are close together on the same chromosome (this is called the coupling phase, the alternative with *G* and *t* together is called repulsion), we would observe departure from Mendelian independent assortment. This is most readily seen in the double backcross type of mating where an individual of genotype *GT/gt* mates with someone of the *gt/gt* genotype. On average, among their offspring, those of the parental types *GT/gt* and *gt/gt* will outnumber those of the types *Gt/gt* and gT/gt where alleles at the two loci have recombined. The number of offspring showing recombination divided by the total number of offspring is called the recombination fraction and, within certain limits, its size is proportional to the physical distance between the two loci. It follows that if the two loci are very widely separated or they are on different chromosomes, the recombination fraction will be one-half. Conversely, if the two loci are extremely close, the recombination fraction tends to zero. The tasks of linkage studies are twofold: to *detect* linkage and to *estimate* the recombination fraction. These are usefully accomplished using a likelihood method of analysis and calculating lod (log of the odds) scores (Morton, 1955). A lod score is the common log of the likelihood that the recombination fraction has a certain value divided by the likelihood that the recombination fraction is 0.5. The lod scores for a particular data set are calculated for a range of values of recombination fraction between zero and 0.5. Where the lod score value is highest provides the maximum likelihood (or 'best bet') estimate of the recombination fraction. Conventionally, lod scores in excess of 3 (odds of 1000 to 1 on linkage) are taken as firm evidence in favour of linkage (Morton, 1955).

Linkage studies using classical autosomal markers such as red cell types (ABO groups, rhesus and Mn systems, etc.), histocompatibility antigens (HLA types), red cell enzymes, and other protein polymorphisms have not yielded consistently positive results (Goldin *et al*, 1983). A serious limitation of classic marker studies is that even where there is good collaboration between laboratories, it is seldom possible to study more than about 30 loci at a time. However, it has been known for some years that the number of markers required to span the entire human genome is perhaps as many as ten times this number. The 'new genetics' of recombinant DNA has resulted in a new generation of markers, restriction fragment length polymorphisms (RFLPs) which exist because of individual differences in the base pair sequences of DNA. A class of bacterial enzymes called restriction endonucleases, which recognise and cleave DNA at specific sites, produce fragments which differ in length between different individuals and can be separated by electrophoresis. Particular fragments can be detected using radio-labelled DNA as probes in the technique called Southern blotting (Southern, 1975). RFLPs segregate as simple Mendelian co-dominants and a sufficient number are now available to form a complete human genetic linkage map (Donis-Keller *et al*, 1987).

Given the whole human gene map to choose from, some authorities have advocated a 'candidate gene' approach. This entails focusing on marker genes where the gene products have some putative relationship with the pathogenesis of the disorder. For example, in affective illness we might focus on probes for catecholamine receptors. However, most interesting findings have recently emerged using RFLPs in random-linkage strategies. Here there is no prior reason for suspecting a relationship between a particular marker and a disease but instead the co-segregation of the disorder and a series of 'randomly' chosen genetic markers is studied in families with two or more affected members. In an investigation of a large pedigree of the Old Order Amish in the USA, strong evidence of linkage was found between a gene for bipolar disorder and the H-ras locus on the short arm of chromosome 11 (Egeland *et al*, 1987). The evidence for linkage here was strong, with a lod score of about 4 representing odds on linkage of 10 000 to 1. Unfortunately, other investigators have not only failed to confirm such a linkage but have effectively excluded it in other North American, Icelandic, and Irish pedigrees (Hodgkinson *et al*, 1987; Detera-Wadleigh *et al*, 1987; Gill *et al*, 1988).

Such findings raise the issue of heterogeneity within bipolar disorder, with some forms linked and other forms not linked to the H-ras locus. One way to test this is to perform the analysis suggested by Morton (1956). Here the null hypothesis is that there is homogeneity within BP disorder with the spurious 'chance positive' appearance of linkage in one or more pedigrees but not in others. On applying Morton's test we find that χ^2 is highly significant, supporting the alternative hypothesis of heterogeneity, i.e. the hypothesis that BP disorder exists in at least two different forms (McGuffin, 1988).

Against this background of probable genetic heterogeneity, there has been a renewed interest in the possibility of X-linkage in some forms of affective illness. X-linked pedigrees were first described two decades ago (Reich *et al*, 1969). X-linkage can at best account for only a minority of inherited forms of affective illness. In some families there is father–son transmission which effectively excludes X-linkage, and various groups have failed to confirm linkage with X chromosome markers (Gershon *et al*, 1980). However, there have been two reports in which X-linkage appears highly probable: Baron *et al* (1987) reported linkage between X-chromosome markers and manic depression in Israeli families, while in Belgium Mendlewicz *et al* (1987) produced evidence of linkage with an X-chromosome polymorphic DNA marker.

While these findings are interesting and provocative, it needs to be established whether the chromosome 11 results have a wider application and whether the linkage findings can be replicated in populations other than a genetically isolated North American community. The X-linkage results also need to be confirmed in independent centres before the case for an X-linked gene can be regarded as proven. Even if independent replication of both findings is achieved, it remains probable that most BP illness is not linked to the X chromosome or the H-ras locus, so that if the linkage strategy is to be comprehensive the net must be cast wide and will probably require a systematic trawl through the human genome.

Unipolar disorder and moderate depression

As we noted at the outset, the classification of depression and our confidence in defining the phenotype becomes less certain as we move nearer to the borderlands between clinical depression and common distress. The subdivision of depression into endogenous and neurotic types has enjoyed greater and more enduring popularity among British and European psychiatrists than among North Americans. A recent multicentre collaborative study in the USA found no difference in the frequency of depressive illness between the relatives of neurotically and endogenously depressed patients (Andreasen *et al*, 1986). This is in marked contrast with earlier Swedish studies of Stenstedt (1952, 1966), which demonstrated high risks of depression in the relatives of typical endogenous probands but a risk of depression of only 5.4% in the relatives of neurotically depressed probands compared with an estimated risk in the general population of about 3% (Stenstedt, 1966). A subsequent Scandinavian study reported a morbid risk of 9% among the first-degree relatives of neurotic depressives (Perris *et al*, 1982).

It could be argued that the Swedish studies deserve less emphasis than the American collaborative study because of small sample sizes and less satisfactory methodology. However, it could also be that the apparent differences in the findings simply reflect differences in the definition of the disorder. A British study in which all available first-degree relatives of 83 depressed probands were interviewed demonstrated that the pattern of results is to a considerable extent dependent upon the breadth of diagnostic criteria used (McGuffin *et al*, 1987). Some of the findings are summarised in Table III. There were actually more currently ill relatives in the families of neurotic probands when the definition of current illness was a broad one based upon

TABLE III

Frequency (%) of depression in the first-degree relatives of probands with neurotic or endogenous depression (from McGuffin et al, *1987)*

	Proband type		*General*
	Neurotic	*Endogenous*	*population*
Prevalence of current 'cases'	23.5	12.7	11.1[1]
Morbid risk of moderate plus severe depression	23.7	25.7	8.9[2]
Morbid risk of severe depression	7.9	14.7	2.6[2]

1. From Bebbington *et al* (1981).
2. From Sturt *et al* (1984).

PSE-ID-CATEGO criteria (Wing *et al*, 1974; Wing & Sturt, 1978). Regarding lifetime risk, there was no difference in the rate of moderate plus severe depression between first-degree relatives of neurotically and endogenously depressed probands. However, when consideration was restricted to severe depression, the rate in first-degree relatives of the endogenous group of probands was 14.7%, nearly twice that in the relatives of neurotic probands. Our conclusions are therefore heavily influenced by what we select as our relevant phenotype.

The overall impression that neurotic disorder is somewhat less genetically influenced than endogenous depression is confirmed by twin studies. However, once again the statement must be qualified by stating that the results are partially dependent on the choice of diagnostic criteria. The results of three published studied are summarised in Table IV. Slater & Shields (1969) found zero concordance for narrowly defined depression in the twins of neurotically depressed probands and, like Torgersen (1985), found little difference between the monozygotic and dizygotic concordances even after taking a much broader diagnostic perspective. By contrast, Shapiro (1971), an American psychiatrist working in Denmark, did find evidence of a substantial genetic contribution to 'non-endogenous' depression. He found higher concordances for depression, whether narrowly or broadly defined, in MZ than in DZ twins. However, it is probable that the probands in Shapiro's series were more severely ill than in the two other twin studies as, unlike the latter, all had been treated as in-patients. Furthermore, Shapiro's series almost certainly included an admixture of probands suffering from what in Denmark is called reactive depressive psychosis but which in other parts of the world might be placed in an 'endogenous' category.

Taken together these data are complex and do not lend themselves to a simple interpretation. Nevertheless, it is reasonable to conclude that even less severe forms of depression show a tendency to aggregate in families, and it is likely that both genes and environment contribute to the aetiology. In typical or severe forms of unipolar depression genetic influences seem to be most important, while in the less severe cases the environment predominates. We will therefore attempt to pursue this line of reasoning further by examining the ways in which genetic and environmental contributions can be quantified, and in which familial and environmental factors can be examined simultaneously.

Environmental adversity and genetic predisposition

Any observed phenotype is due to a combination of the genotype and the environment to which the genotype is exposed. If we have a phenotype such as depression that shows variability in the population and if, for the purposes of simplicity, we assume that there is no gene-environment covariance and that there are no non-additive gene-environment interactions, then the variance in the phenotype is a simple additive combination of the variance due to genes and the variance due to environmental

TABLE IV

Twin studies of neurotic or non-endogenous depression

Authors	*Monozygotic*		*Dizygotic*	
	No. of probands	*Probandwise concordance: % (narrow/broad criteria)*	*No. of probands*	*Probandwise concordance: % (narrow/broad criteria)*
Slater & Shields (1969)	8	0/38	16	0/25
Shapiro (1971)	18	22/55[1]	14	0/14[1]
Torgersen (1985)	17	36/53	33	33/45

1. In Shapiro's study, narrow concordance = cotwin hospitalised with depression, broad concordance = any form of treated depression in cotwin. In the two other studies, narrow = depression in cotwin, broad = any psychiatric disorder.

factors. We can complicate this simple scheme by dividing the environment into a component shared within families and another component specific to the individual. Thus, two main factors can contribute to the familiality of depression, genes and common environment. If we assume that liability to depression is made up of predominantly additive genetic and environmental effects and is normally distributed within the population (or can be transformed to normal) we can attempt to estimate the value of two parameters. Heritability (h^2) is the proportion of total phenotypic variance contributed by additive gene effects, while c^2 denotes the proportion of variance contributed by common family environment. Given probandwise concordances for MZ and DZ twins, together with an estimate of a population frequency of depression, it is possible to calculate correlations in liability (Reich *et al*, 1972), and having done this it is a relatively simple matter to estimate h^2 and c^2 (McGuffin & Katz (1986), and see Smith (1974) for calculation of standard errors).

Table V presents three sets of twin data, with estimates of the components of variance in liability to affective illness. It is clear that genes provide an overwhelming contribution to severe typical manic–depressive illness as studied by Bertelsen *et al* (1977), accounting for over 80% of the variance in liability. By contrast, neurotic depression receives a large contribution from family environment, with a c^2 of 54%, and a comparatively trivial contribution from genes. Using the DSM–III concept of major depression, in our own study we obtain results roughly midway between those for the two classical disorders of manic–depressive illness and neurotic depression. Here genes contribute approximately half of the variance in liability with just under a third due to common family environment. This midway position of major depression is perhaps scarcely surprising in view of our own experience that this category consists of a mixture of what ICD–9 defines as manic–depressive illness, depressed type, and depressive neurosis (World Health Organization, 1978).

Therefore, we can take it that classic manic–depressive illness is highly heritable and is an appropriate focus for molecular genetic endeavours, but beyond this we can take little overall satisfaction in methods of delineating categories of depression. The process of classifying diseases is said to be an attempt to carve nature at the joints. Here we appear to have different methods of slicing up a salami, albeit revealing more genetic content at one end and more environmental filling at the other.

There are further reasons for caution in interpreting heritability estimates. Not least of these in this instance are the very large standard errors attached to the figures in Table V. It is important to remember that heritability is a population parameter which does not necessarily have any applicability in populations other than the one from which the estimate was obtained. Furthermore, heritability has no meaning at an individual level. Nevertheless, estimates of h^2 and c^2, providing these limitations are accepted, can act as a useful starting point for considering the ways in which genes and environment may produce the depressive phenotype.

It is now well established that certain forms of adversity, such as life events that carry a severe or moderately severe threat, have a strong association with onset of depression (Brown & Harris, 1978; Bebbington, 1985). Unfortunately, there have been few attempts to study environmental stress and familial/genetic factors in the same population. Pollitt (1972) was among the first to attempt to remedy this. He found that the morbid risk of depression among relatives of depressed probands whose illness arose 'out of the blue' was higher, at about 21%, than when the proband's illness was 'justifiable' (e.g. following severe physical stress of psychological trauma), at about 6–12%.

More sophisticated methodologies are now available for studying 'stress' in relation to mental

TABLE V

Contributions to the variance in liability: calculations based on recent twin studies of depression

	h^2 *(additive genetic)*	c^2 *(common environment)*	s^2 *(non-shared environment)*	*Kp: %* *(population risk)*
Manic–depressive illness (Bertelsen *et al*, 1977)	0.86	0.07	0.07	3.0
Major affective disorder (McGuffin & Katz, preliminary data)	0.52	0.30	0.18	4.7
Neurotic depression (Torgersen, 1986)	0.08	0.54	0.38	6.0

illness (Brown & Harris, 1978; Paykel, 1978; Bebbington, 1985). In a collaborative investigation between the Sections of Genetics and Social Psychiatry at the Institute of Psychiatry, Maudsley Hospital, 83 families identified via depressed probands from Camberwell were studied in detail (Bebbington *et al*, 1988; McGuffin *et al*, 1988*a,b*), and a number of unexpected findings emerged. Depression was no more common among the relatives of probands whose illness was not in any discernible way 'reactive' than among the relatives of probands whose depression followed adversity. Furthermore, the frequency of reported life events showed a highly significant increase among the relatives of depressives compared with a sample from the general population. This finding held even when proband-associated events were discounted. Within families exposure to life events showed only a weak and non-significant association with depression. The findings suggest the possibility that event-associated depression is something which occurs in hazard-prone rather than just stress-susceptible individuals. Furthermore, it seems possible that part of the association between life events and depression, which has been consistently shown in previous studies, is due to the fact that both show familial aggregation (McGuffin *et al*, 1988*b*).

The Camberwell family study suggests that the relationship between life stress and depressive diathesis is complex and that a better understanding of the underlying personality variables is required. Unfortunately, preliminary analyses of personality measures on these family data suggest that the alleged trait measure of emotional instability or 'neuroticism' is actually closely associated with the mental states encountered in clinical practice and that the trait and state are often confounded (Katz & McGuffin, 1987). Neuroticism scores were highest in family members who were currently depressed, lowest in those who had never suffered depression, and intermediate in those who had been depressed in the past but who, on current examination, were well.

Bearing in mind our speculations about the continuity between clinical depression and 'normal' symptoms, one approach to the problem is to study personality traits and symptoms of anxiety or depression in volunteer twins. Kendler *et al* (1986) studied a large sample from the Australian Medical Research Council Register. They found strong evidence that genetic factors contribute to symptoms of anxiety and depression as reported in the general population. Subsequently, multivariate analyses suggested that genes act in a fairly general way, with no evidence of a specific influence on symptoms of depression rather than symptoms of anxiety (Kendler *et al*, 1987). However, it was found that certain environmental features seem to influence symptoms of anxiety but have little impact on symptoms of depression. These are intriguing results but at present it is not clear to what extent the findings can be extrapolated to clinical populations.

Sex differences

It is not possible to give an adequate account of the complex relationship between genes and environment in the aetiology of depression without taking sex differences into consideration. Virtually all family studies have been in agreement with epidemiological studies in finding more women than men affected by depression (Reich *et al*, 1982). The excess of women is, however, minimal or even absent in studies of BP disorder.

Broadly, two types of explanation have been offered for sex differences in the frequency of depression: biological and environmental. The most provocative biological theory has, of course, been that dominant X-linked genes explain the higher risk in women. However, as we have discussed earlier, X-linkage can, at best, account for the transmission of only a small proportion of cases of familial affective disorder, mainly where the probands have BP illness. A more comprehensive approach was adopted by Rice *et al* (1984) in their analysis of data from a multicentre collaborative study of depression in the United States. Applying a liability threshold model of sex differences, it was found that the data were compatible with a higher mean liability towards depression for women than men which appeared to be due to systematic biological/cultural differences, with parental transmission contributing to variation about the means. The data were held to be incompatible with the hypothesis that women simply have a lower threshold for reporting depressive symptoms. Furthermore, a 'cohort effect' was observed so that the sex ratio was close to unity among younger age groups. Other recent American family studies concur in finding only a modest sex difference in the frequency of affective disorder within families (Gershon *et al*, 1982; Weissman *et al*, 1984).

Unfortunately, any such conclusion is dependent on the methods of classification, and the importance of the way in which the phenotype is defined is again underlined by the recent Camberwell family studies (Bebbington *et al*, 1988; McGuffin *et al*, 1988*a*). Here it was found that there were significantly higher rates of depression among female than among male first-degree relatives for broader categories of disorder, but there was a small and non-significant excess of men among those relatives who had received in-patient treatment for depression (McGuffin *et al*, 1988*a*). This lessening of the sex difference with apparently more severe forms of the disorder is a frequent finding in the literature (Bebbington, 1987). However, it did not apply when lifetime prevalence of illness based on reported symptoms was examined. Thus, for example, 35% of women and only 14% of men reported having symptoms at some stage in their lives taking them into the definite case category with a PSE–CATEGO–ID level of six or greater.

The observed discrepancy between sex differences in depression when self-report is compared with less subjective criteria (i.e. referral to hospital) raises some intriguing questions. Do women have a tendency to volunteer more symptoms? (despite suggestions to the contrary by Rice *et al* (1984))? Conversely, do men have a tendency to under-report or tone down past or present feelings of depression? If this is the case, it appears that doctors, at least those in Britain, compensate by adopting a lower threshold for psychiatric referral when faced with depressive symptoms in a man.

Overall the findings from our own study, taken together with evidence of secular changes (Klerman *et al*, 1985), of less marked sex differences in developing countries (e.g. Orley & Wing, 1979), and of minimal difference in prevalence of symptoms once employment status and other social factors are taken into account (Jenkins, 1985), lead us to conclude that most of the differences between the sexes in respect of prevalence of depression are due to environmental factors.

Conclusions

There is consistent and compelling evidence for genetic contribution to typical manic–depressive illness. Genetic studies provide a firm foundation for the conviction that there is a biological basis of depression and the analysis of twin data suggests that the magnitude of the contribution is very substantial, accounting for about 80% of the variance in liability. Other statistical studies provide suggestions of major gene effects, and there has been a (so far unreplicated) report of linkage between the gene for manic–depressive illness and a DNA marker on chromosome 11 as well as multiple reports of X-linkage. Eliciting the molecular genetic basis of manic–depressive illness should prove to be one of the great challenges of the next decade.

The other focus of current interest lies nearer to the opposite end of the complex pathway between abnormal genes and abnormal behaviour. Studies of the ways in which phenotypes can be most usefully defined, and of the ways in which genes and environment co-act and interact to produce depression, are of foremost importance. Most of this work focuses on unipolar disorder, which continues to present classificatory problems for the researcher and the clinician alike (Kendell, 1976; Farmer & McGuffin, 1989). Nevertheless, it is clear that most forms of depression seem to be familial. The genetic contribution appears to be greater with the more severe disorders while it is likely that environmental factors play a more prominent role in milder conditions. However, the interplay between genes and environment is complex, and McGuffin *et al* (1988*b*), investigating familiality and adversity in the same sample, failed to show a simple inverse relationship between the degree to which depression is secondary to threatening life events and the degree of family loading. Instead, it was found that both depression and threatening life events tend to cluster in families, and so it is possible that a liability to develop depressive illness and propensity to experience (or to report) unpleasant life events are different manifestations of the same familial diathesis.

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References

American Psychiatric Association (1980) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn) (DSM–III). Washington, DC: APA.

Andreasen, N. C., Rice, J., Endicott, J., *et al* (1986) The family history approach to diagnosis. *Archives of General Psychiatry*, **43**, 421–429.

Angst, J. (1966) *Zur Atiologie und Nosologie endogener depressiver Psychosen*. Monographen ans der Neurologie und Psychiatrie N.112. Berlin: Springer.

Baron, M., Risch, N., Hamburger, R., *et al* (1987) Genetic linkage between X chromosome markers and manic depression. *Nature*, **326**, 806–808.

Bebbington, P. (1985) Psychosocial etiology of schizophrenia and affective disorders. *Psychiatry* (ed. R. Michels). Philadelphia, Pennsylvania: Lippincott.

—— (1987) The social epidemiology of clinical depression. In *Handbook of Studies on Social Psychiatry* (eds A. S. Henderson & G. Burrows). Amsterdam: Elsevier.

——, Hurry, J., Tennant, C., *et al* (1981) Epidemiology of mental disorders in Camberwell. *Psychological Medicine*, **11**, 561–579.

——, Brugha, T., MacCarthy, B., *et al* (1988) The Camberwell Collaborative Depression Study. I. Depressed probands: adversity and the form of depression. *British Journal of Psychiatry*, **152**, 754–765.

——, Katz, R., McGuffin, P., *et al* (1989) The risk of minor depression before age 65: results from a community survey. *Psychological Medicine*, (in press).

Bertelsen, A., Harvald, B. & Hauge, M. (1977) A Danish twin study of manic–depressive disorders. *British Journal of Psychiatry*, **130**, 330–351.

Brown, G. W. & Harris, T. (1978) *The Social Origins of Depression*. London: Tavistock.

Cadoret, R. (1978) Evidence for genetic inheritance of primary affective disorder in adoptees. *American Journal of Psychiatry*, **133**, 463–466.

Detera-Wadleigh, S. D., Berretin, W. H., Goldin, L. R., *et al* (1987) Close linkage of C-Harvey ras-1 and the insulin gene to affective disorder is ruled out in three North American pedigrees. *Nature*, **325**, 806–807.

Eastwood, M. R. & Kramer, P. M. (1981) Epidemiology and depression (editorial). *Psychological Medicine*, **11**, 229–234.

Egeland, J. A., Gerhard, D. S., Pauls, D. L., *et al* (1987) Bipolar affective disorder linked to DNA markers on chromosome 11. *Nature*, **325**, 783–787.

Falconer, D. S. (1965) The inheritance of liability to certain diseases estimated from the incidence among relatives. *Annals of Human Genetics*, **29**, 51–59.

—— (1981) *Introduction to Quantitative Genetics* (2nd edn). London: Longman.

Farber, S. L. (1981) *Identical Twins Reared Apart*. New York: Basic Books.

Farmer, A. E. & McGuffin, P. (1989) Classification of the depressions: Contemporary confusion revisited. *British Journal of Psychiatry* (in press).

Gershon, E. S., Mark, A., Cohen, N., *et al* (1975) Transmitted factors in the morbid risk of affective disorders. *Journal of Psychiatric Research*, **12**, 283–299.

——, Mendlewicz, J., Gastpar, M., *et al* (1980) A collaborative study of genetic linkage of bipolar manic depressive illness and red/green colour blindness. *Acta Psychiatrica Scandinavica*, **61**, 319–338.

——, Hamovit, J., Groff, J. J., *et al* (1982) A family study of schizoaffective bipolar I, bipolar II, unipolar and normal control probands. *Archives of General Psychiatry*, **39**, 1157–1167.

Gill, M., McKeon, P. & Humphries, P. (1988) Linkage analysis of manic depression in an Irish family using H-ras 1 and INS DNA markers. *Journal of Medical Genetics*, **25**, 634–637.

Goldin, L. R., Gershon, E. S., Targum, S. D., *et al* (1983) Segregation and linkage analyses in families of patients with bipolar, unipolar and schizoaffective mood disorder. *American Journal of Human Genetics*, **35**, 274–288.

Hodgkinson, S., Sherrington, R., Gurling, H. M. D., *et al* (1987) Molecular genetic evidence for heterogeneity in manic depression. *Nature*, **325**, 805–806.

James, J. (1971) Frequency in relatives for an all-or-none trait. *Annals of Human Genetics*, **35**, 47–49.

Jenkins, R. (1985) Sex differences in minor psychiatric morbidity. *Psychological Medicine* (monograph, suppl. 7).

Katz, R. & McGuffin, P. (1987) Neuroticism in familial depression. *Psychological Medicine*, **17**, 155–161.

Kendell, R. E. (1976) The classification of depression: a review of contemporary confusion. *British Journal of Psychiatry*, **129**, 15–28.

Kendler, K. S., Heath, A. C., Martin, N. G., *et al* (1986) Symptoms of anxiety and symptoms of depression. *Archives of General Psychiatry*, **44**, 451–457.

——, ——, ——, *et al* (1987) Symptoms of anxiety and symptoms of depression. *Archives of General Psychiatry*, **44**, 451–457.

Klerman, G. L., Lavori, P. N., Rice, J., *et al* (1985) Birth cohort trends in rates of major depressive disorder among relatives of patients with affective disorder. *Archives of General Psychiatry*, **42**, 689–693.

Lalouel, J. M., Rao, D. L., Morton, N. E., *et al* (1983) A unified model for complex segregation analysis. *American Journal of Human Genetics*, **35**, 816–826.

Leonhard, K. (1959) *Aufteilung der Endogen Psychosen*. Berlin: Akademic Verlag.

McGuffin, P. (1988) Major genes for major affective disorder. *British Journal of Psychiatry*, **153**, 591–596.

—— & Katz, R. (1986) Nature, nurture and affective disorder. In *The Biology of Depression* (ed. J. W. F. Deakin), pp. 26–51. London: Gaskell.

——, —— & Bebbington, P. (1987) Hazard, heredity and affective disorder. A family study. *Journal of Psychiatric Research*, **21**, 365–375.

——, ——, Aldrich, J., *et al* (1988*a*) The Camberwell Collaborative Depression Study. II. Investigation of family members. *British Journal of Psychiatry*, **152**, 766–775.

——, —— & Bebbington, P. (1988*b*) The Camberwell Collaborative Depression Study. III. Depression and adversity in the relatives of depressed probands. *British Journal of Psychiatry*, **152**, 775–782.

Mendlewicz, J. & Rainier, J. D. (1977) Adoption study supporting genetic transmission in manic–depressive illness. *Nature*, **268**, 326–329.

——, Simon, P., Sevy, S., *et al* (1987) Polymorphic DNA marker and X chromosome and manic depression. *Lancet*, *ii*, 1230–1232.

Morton, N. E. (1955) Sequential tests for the detection of linkage. *American Journal of Human Genetics*, **7**, 277–318.

—— (1956) The detection and estimation of linkage between the genes for elliptocytosis and Rh blood type. *American Journal of Human Genetics*, **8**, 80–96.

—— (1982) *Outline of Genetic Epidemiology*. Basel: Karger.

—— & Maclean, C. J. (1974) Analysis of familial resemblance. III. Complex segregation analysis of quantitative traits. *American Journal of Human Genetics*, **26**, 489.

Orley, J. & Wing, J. K. (1979) Psychiatric disorders in two African villages. *Archives of General Psychiatry*, **36**, 513–520.

O'Rourke, D. H., McGuffin, P., Reich, T. (1983) Genetic analysis of manic–depressive illness. *American Journal of Physical Anthropology*, **62**, 51–59.

Paykel, E. S. (1978) Contribution of life events to causation of psychiatric illness. *Psychological Medicine*, **8**, 245–253.

Perris, C. (1966) A study of bipolar (manic depressive) and unipolar recurrent depressive psychoses. *Acta Psychiatrica et Neurologica Scandinavica* (suppl. 42).

——, Perris, H., Ericsson, U., *et al* (1982) The genetics of depression. A family study of unipolar and neurotic reactive depressed patients. *Archives für Psychiatrica Nervenkranken*, **232**, 137–155.

Pollitt, J. (1972) The relationship between genetic and precipitating factors in depressive illness. *British Journal of Psychiatry*, **121**, 67–70.

Price, J. (1968) The genetics of depressive behaviour. In *Recent Developments in Affective Disorders* (eds A. J. Coppen & A. Walk), British Journal of Psychiatry, Special Publication No. 2. Ashford: Headley Bros.

Reich, T., Clayton, P. J. & Winokur, G. (1969) Family history studies V. The genetics of mania. *American Journal of Psychiatry*, **125**, 1358–1369.

——, James, J. W. & Morris, C. A. (1972) The use of multiple thresholds in determining the mode of transmission of semi-continuous traits. *Annals of Human Genetics*, **36**, 163–184.

——, Cloninger, C. R., Suarez, B., *et al* (1982) Genetics of the affective disorders. In *Handbook of Psychiatry, vol. III, Psychosis of Uncertain Aetiology* (eds J. K. Wing & L. Wing). Cambridge: Cambridge University Press.

Rice, J., Reich, T., Andreasen, N. C., *et al* (1984) Sex related differences in depression–familial evidence. *Journal of Affective Disorders*, **7**, 199–210.

——, ——, ——, *et al* (1987) The familial transmission of bipolar illness. *Archives of General Psychiatry*, **44**, 441–447.

Shapiro, R. W. (1971) A twin study of non-endogenous depression. *Acta Jutlandica*, **42** (publication of the University of Aarhus).

Slater, E. & Shields, J. (1969) Genetical aspects of anxiety. In *Studies of Anxiety* (ed. M. H. Lader), British Journal of Psychiatry, Special Publication No. 3. Ashford: Headley Bros.

—— & Cowie, V. (1971) *The Genetics of Mental Disorder*. London: Oxford University Press.

Smith, C. (1974) Concordance in twins: methods and interpolation. *American Journal of Human Genetics*, **26**, 454–466.

Southern, E. M. (1975) Detection of specific sequences among DNA fragments separated by gel electrophoresis. *Journal of Molecular Biology*, **98**, 503–517.

STENSTEDT, A. (1952) A study in manic depressive psychosis: clinical, social and genetic investigations. *Acta Psychiatrica Scandinavica* (suppl. 79).

—— (1966) Genetics of neurotic depression. *Acta Psychiatrica Scandinavica*, **42**, 392–409.

TORGERSEN, S. (1986) Genetic factors in moderately severe and mild affective disorders. *Archives of General Psychiatry*, **43**, 222–226.

STURT, E., KUMAKARA, N. & DER, G. (1984) How depressing life is – lifelong morbidity risk for depressive disorder in the general population. *Journal of Affective Disorder*, 7, 109–122.

TSUANG, M., WINOKUR, G. & CROWE, R. (1980) Morbidity risks of schizophrenia and affective disorders among first degree relatives of patients with schizophrenia, mania, depression and surgical conditions. *British Journal of Psychiatry*, **137**, 497–504.

VON KNORRING, A. L., CLONINGER, C. R., BOHMAN, N., *et al* (1983) An adoption study of depressive disorders and substance abuse. *Archives of General Psychiatry*, **40**, 843–950.

WEISSMAN, M. M., GERSHON, E., KIDD, K. K., *et al* (1984) Psychiatric disorders in the relatives of probands with affective disorders. *Archives of General Psychiatry*, **41**, 13–21.

WENDER, P. H., KETY, S. S., ROSENTHAL, D., *et al* (1986) Psychological disorders in the biological and adoptive relatives of individuals with affective disorders. *Archives of General Psychiatry*, **43**, 923–929.

WING, J. K., COOPER, J. E. & SARTORIUS, N. (1974) *The Measurement and Classification of Psychiatric Symptoms*. Cambridge: Cambridge University Press.

—— & STURT, E. (1978) *The PSD–ID–CATEGO System Supplementary Manual* (mimeo). London: Medical Research Council.

WORLD HEALTH ORGANIZATION (1978) *Mental Disorders: Glossary and Guide to their Classification in Accordance with the Ninth Revision of the International Classification of Diseases* (ICD-9). Geneva: WHO.

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Review Article

Beyond the Dopamine Hypothesis

The Neurochemical Pathology of Schizophrenia

G. P. REYNOLDS

The dopamine hypothesis still provides a valuable approach to the study of schizophrenia and its treatment by drugs. Although the neuroleptic drugs appear to act via an inhibition of dopamine receptors, measurements of dopamine metabolites *in vivo*, or of the transmitter and its receptors in post-mortem brain tissue, do not provide unequivocal evidence of a hyperactivity of dopaminergic neurotransmission in the disease. Nevertheless, increased dopamine function might be a consequence of a primary neuronal abnormality in another system. Recent imaging studies and neuropathological reports suggest that, in some patients, there may be a deficit and/or disturbance of neurons in certain temporal limbic regions, and this is supported by some neurochemical investigations, particularly of neuropeptide and amino-acid transmitter systems. A loss of such neurons could conceivably lead to a disinhibition of limbic dopamine neurons, providing the means whereby neuroleptic drug treatment might ameliorate the effects of a neuronal deficit in schizophrenia.

Biological research in schizophrenia is undoubtedly undergoing a renaissance. The advent and development of tomographic imaging techniques has led to the *in-vivo* identification of cerebral abnormalities of structure and/or metabolic activity in a disease which, but a few years ago, had yielded little direct evidence for any organic disturbance whatsoever. Thus the distinction between 'functional' and 'organic' psychotic disorders, which descriptions imply differences in aetiology and mechanism, has become blurred. In fact, the prevailing view in biological psychiatry is that schizophrenia is "no longer a functional psychosis" (Tyrer & Mackay, 1986).

Classic neuropathological studies have, until recently, been unsuccessful in identifying consistent and accepted indicators of any neuronal dysfunction in schizophrenia. However, the increasing evidence obtained from imaging is strongly suggestive of a neuronal pathology in the disease. This will inevitably be reflected by a neurochemical pathology, since neuronal activity is, in simple terms, mediated by neurotransmitter synthesis, release, and receptor response. Almost every neurotransmitter has, at some stage, been proposed to be the key neurochemical factor in schizophrenia (and these have been assessed in recent reviews elsewhere, e.g. Owen & Crow (1987), Kleinman *et al* (1988), Reynolds (1988)). However, this article will not attempt a comprehensive discussion of these theories except where they impinge upon recent neuroanatomical and histopathological findings and the dopamine hypothesis of the disease. It is intended to review the present status of this major biochemical theory of schizophrenia and, by integrating this information with results from other neurochemical investigations, as well as from recent neuropathological and pharmacological studies, to describe a tentative neurochemical pathology of schizophrenia.

The dopamine hypothesis

The premises on which neurochemical theories of schizophrenia have been built have never been very firm. Over the past few decades there has been no shortage of hypotheses for the aetiological abnormality of schizophrenia based on one or other neurotransmitter system. As well as over- or underproduction of transmitters and hyper- or hypoinnervation in various pathways, deficits of metabolic enzymes and aberrant production of psychotomimetics have all been proposed, albeit on the basis of purely circumstantial, and often very tenuous, evidence. While each hypothesis has its supporting data, it has proved very difficult to obtain consistent and reproducible results indicating a specific neurochemical difference in the brains of schizophrenic patients.

Despite these difficulties, dopamine has remained a major candidate for the primary neurotransmitter involvement in schizophrenia since it was first proposed over 20 years ago. This 'dopamine hypothesis' developed from the role of the transmitter in the action of amphetamine, which can induce paranoid schizophreniform psychosis (Randrup & Munkvad, 1965; Snyder *et al*, 1974). The greatest support comes from the substantial evidence for a blockade of dopaminergic neurotransmission being an action common to the neuroleptic drugs. Thus the dopamine D2 receptor blockade induced by these compounds is the one pharmacological effect which clearly correlates with their clinical antipsychotic dosage (Creese *et al*, 1975; Seeman *et al*, 1976). This, of course, points particularly well to the site of antipsychotic action but again provides no direct evidence for dopamine involvement in schizophrenia.

So the search continues for an abnormality affecting dopamine neurotransmission in schizophrenic patients. The positive findings have been sparse when one eliminates the many inconsistent, irreproducible and artifactual results. To take just one example, the enzyme responsible for most breakdown of dopamine and other monoamine neurotransmitters, monamine oxidase (MAO), has been much investigated, although many of the reported differences in blood platelets (which, even if they reflected changes in the brain, were probably too small to induce any change in central dopamine concentrations) could be put down to the effects of neuroleptic drug treatment (De Lisi *et al*, 1982). This problem of distinguishing drug effects from those of the disease process appears as a recurring theme throughout neurochemical research in schizophrenia.

The 'window on the brain' provided by neuroendocrine studies has been used to assess dopamine function in schizophrenia by investigating growth hormone and prolactin; the secretion of both these hormones are influenced by dopamine transmission. While some interesting results have been obtained (and recently reviewed by Cleghorn & Brown (1988)) there is little to suggest that the group of dopamine neurons affecting the release of these hormones is important in schizophrenia. More strongly implicated are the far more numerous midbrain neurons that project to the striatum and to the cortex and limbic brain. It is with these systems that this review is concerned.

In-vivo assessment of central dopamine metabolism

Dopamine metabolites in CSF

One approach to understanding the neurochemical pathology of schizophrenia has been the investigation of body fluids in order to identify changes in cerebrospinal fluid (CSF), blood or urine which reflect differences of activity of transmitters such as dopamine in the central nervous system. This is perhaps easier to justify in the case of CSF than it is for blood or urine, although both blood plasma and CSF have frequently been taken from psychiatric patients for the analysis of monoamine transmitters and their metabolites. In particular homovanillic acid (HVA), which in man is the major metabolite of dopamine, has been much studied in this way. Thus the closest assessment of dopamine function *in vivo* has classically been the measurement of HVA in CSF. This is considered to provide a measure of central dopamine turnover, and hence dopaminergic activity in the brain. One of the earlier studies found, for example, reduced levels of HVA in CSF in schizophrenics as compared with a control group (with affective disorder) (Bowers, 1974). This study was performed after pre-treatment of the patients with probenecid, allowing the HVA to accumulate by blocking its output from the CSF. The effect of neuroleptic administration on these patients was to increase HVA concentrations. The deficit of HVA was most apparent in what was defined as a 'typical' subgroup of patients (i.e. with a poor prognosis), a finding for which more recent studies may provide an explanation.

Van Kammen *et al* (1983) found that CSF levels of HVA were lower in those schizophrenic patients with cerebral atrophy, and other groups (Losconczy *et al*, 1986; Doran *et al*, 1987) have reported similar relationships between CSF HVA and ventricular volume or frontal atrophy. It is tempting to suggest that the apparent relationship with clinical features observed by Bowers and other groups may well relate to cerebral atrophy occurring to a greater degree in the patients with poor prognosis.

Why should there be this relationship between cerebral atrophy and HVA concentrations in the CSF? There are reports from both animal (Elsworth *et al*, 1987) and post-mortem human (Stanley *et al*, 1985) studies that there is a correlation between CSF and cortical brain concentrations of HVA. This is interpreted as indicating that CSF HVA reflects cortical dopamine metabolism. Thus a reduction in cortical dopamine may occur in schizophrenia, brought about by cerebral atrophy. But post-mortem studies do not provide evidence for such a reduction; in fact an increase in HVA has been observed (Bacopoulos *et al*, 1979*b*; Reynolds & Czudek, 1988), as discussed below. Nevertheless there are other, simpler explanations to be considered. An increase in the ventricular volume will inevitably mean an increase in the amount of CSF. Since the CSF HVA concentration is not constant but exhibits ventricular–lumbar gradients (as manifested by the differences in consecutive aliquots from a single puncture), an increase in ventricular volume would inevitably perturb this dynamic equilibrium. A decrease in the concentration of HVA (and many other brain metabolites) could well be a consequence. Certainly the 5-HT metabolite, 5-HIAA, is also found to be diminished in correlation with increased ventricular size in schizophrenia (Potkin *et al*, 1983).

Plasma HVA

This particular problem of interpretation of CSF biochemistry is avoided by investigations in the periphery, although the measurement of HVA in the plasma is unlikely to reflect cerebral dopaminergic activity quite as well as CSF concentrations. Plasma HVA has been shown to be of heuristic interest, at least, in the study of schizophrenia and the action of antipsychotic drugs. About half the HVA present in plasma is considered to derive from the brain and so, under conditions of dietary control which minimise exogenous contributions to plasma HVA, its determination can provide a reflection of brain HVA output.

As with the CSF studies, plasma HVA has been reported as both increased (Bowers & Swigar, 1987) and diminished (Davidson & Davis, 1988) in schizophrenia, although these inconsistencies may reflect differences in patients with regard to symptoms or medication. Thus the latter group have interpreted a plasma HVA deficit in treatment-resistant patients in terms of a cortical 'hypodopaminergia' and related this to other studies indicating frontocortical dysfunction.

Treatment with neuroleptic drugs has substantial effects on plasma HVA which appear to reflect changes in brain dopaminergic activity. An acute increase (over hours or days) in dopamine metabolism occurs after neuroleptic administration (Davidson *et al*, 1987), reflecting the increased turnover in response to receptor blockade, while in the longer term (weeks) a decrease in plasma HVA is seen, manifesting the development of tolerance (in most dopaminergic neurons) to this effect (Pickar *et al*, 1986). This apparent tolerance to the effects of neuroleptic drugs which is shown by plasma HVA is reminiscent of the changes in subcortical, particularly striatal, dopaminergic activity. In animal experiments it is these regions, and not the cortex, which demonstrate a return to normal HVA concentrations after chronic neuroleptic administration. More directly, correlations between caudate and plasma HVA have been found (Bacopoulos *et al*, 1979*a*), suggesting that the study of plasma HVA in schizophrenia provides an indication of striatal HVA output.

Several groups have shown a relationship between response to treatment, psychotic symptoms, and plasma HVA concentration. Thus global severity of illness correlates with HVA levels (Davis *et al*, 1985), and the decrement in plasma HVA following chronic fluphenazine administration correlates positively with both the rating of psychosis and the patient's response to treatment (Pickar *et al*, 1984). There have been further indications that increased levels of HVA reflect severity of illness in schizophrenic patients and that changes in plasma HVA levels predict response to neuroleptic drugs (Davila *et al*, 1988). While it seems that these results provide some support for the dopamine hypothesis, the neurochemical mechanisms involved are far from clear. Nevertheless, it may be that an eventual decrease in central (particularly subcortical) dopamine turnover is a necessary concomitant of successful antipsychotic drug treatment.

Dopamine and the basal ganglia

It is in post-mortem studies of the brain that the greatest direct support for the dopamine hypothesis has been obtained. These have inevitably concentrated on the regions of the basal ganglia and nucleus accumbens, which contain the vast majority of dopamine in the human brain. However, a range of dopaminergic measures, including concentrations of the transmitter itself, its metabolites, and various associated enzymes, investigated in the brain in schizophrenia have yielded few consistent changes. There have been occasional reports of increased dopamine in the caudate and accumbens nuclei (Bird *et al*, 1979; Mackay *et al*, 1982) although this has not been observed by all groups (Crow *et al*, 1981; Reynolds *et al*, 1987). Nor is there any increase in schizophrenia of the number of dopamine uptake sites, which provide a potential measure of the number of dopaminergic synaptic terminals (Czudek & Reynolds, 1989).

Striatal dopamine receptors

First reported by Owen *et al* (1978) and Lee *et al* (1978), the finding of increased numbers of dopamine receptor sites served to refocus attention on the dopamine hypothesis of schizophrenia. Using the then newly developed technique of radioligand binding, they employed tritium-labelled drugs (spiperone and haloperidol) to measure the density of the neuroleptic-sensitive D2 subtype of dopamine receptors in putamen, caudate, and accumbens tissue taken post-mortem from schizophrenic patients.

The increases found in all these regions were proposed as the primary pathology of the disease, resulting in an overactivity of dopaminergic synapses in the brain which would clearly be ameliorated by the neuroleptic drugs. One major problem, that animal studies demonstrated an increase in D2 receptors which could be brought about by chronic administration of antipsychotic drugs (e.g. Clow *et al*, 1980), was thought to be answered by the finding of a few patients who were apparently drug-free and yet still had elevated receptor density. However, some subsequent studies by other groups (Reynolds *et al*, 1981; Mackay *et al*, 1982) have concluded that the increase in receptors was an effect of chronic treatment with neuroleptics and unrelated to the disease process, since they were unable to identify it in those patients untreated for some months before death. Despite substantial effort to solve this problem by, for example, assessing receptor number in non-schizophrenic, neuroleptic-treated groups of patients, it remained a point of considerable controversy whether the increase in receptors in post-mortem brain tissue bears any relation to the disease process *per se*. This impasse lasted until the recent development of positron emission tomography (PET), which has been employed to determine brain D2 receptor density in living subjects.

PET is an imaging technique which has been used increasingly in recent years to study the brain in schizophrenia, particularly to investigate regional differences in blood flow and in cerebral energy metabolism. Its application to the study of neurotransmitter receptors depends on the injection of a positron-emitting radioligand which will bind specifically to the receptor under investigation. Thus ^{11}C-labelled *N*-methylspiperone and raclopride have been employed to identify binding to dopamine D2 receptors, although the extrapolation from this binding to obtain receptor density is not a simple procedure.

Unfortunately, PET studies of D2 receptors in unmedicated patients have not provided us with a totally unequivocal answer (Waddington, 1989). While one report (Wong *et al*, 1986) described an increase in receptor density in 'drug-naive' schizophrenic patients, a Swedish group employed a more straightforward technical approach to show no increase in D2 sites in younger patients on first admission (Farde *et al*, 1987). Using another imaging technique, employing the gamma-emitter ^{77}Br-bromospiperone, Crawley *et al* (1986) found a small, but significant, increase of 11% in patients untreated for at least six months. However, there have been suggestions (Zeeberg *et al*, 1988) that the data in the paper of Wong *et al* (1986) could be interpreted to yield a different conclusion, and it is becoming more apparent that any increase of D2 receptor density is unlikely to be of *primary* aetiological importance in schizophrenia.

Two further observations add to the interest generated by the study of brain D2 receptors in schizophrenia. One is that from Seeman *et al* (1984) who, with an accumulation of about 70 samples of striatal brain tissue collected post-mortem from schizophrenic subjects, demonstrated a bimodal distribution for dopamine receptor density. This interesting result is open to several possible interpretations which, in the absence of well documented clinical data for these cases, remain no more than speculations. In the light of the above indications that increased D2 receptors relate to prior neuroleptic drug treatment, it seems possible that of the two groups with either high, or near-normal, receptor number, it is only the former who respond to drug treatment in this way. Secondly, one preliminary study has found a hemispheric asymmetry of these receptors in the human brain which is accentuated in schizophrenia (Reynolds *et al*, 1987). The receptor density in the putamen is 19% higher in the right than in the left hemisphere in schizophrenics, substantially greater than in control subjects, thus providing a potential neurochemical basis for the asymmetries of movement that other workers have observed. In particular, these results present a clear correlate of the report of Bracha (1987), who found unmedicated schizophrenic patients tended to turn to the left more than control subjects, and which is consistent with a higher right striatal dopaminergic activity that could be brought about by the observed asymmetry of D2 receptor density. What is unclear is whether the effect is associated with prior neuroleptic treatment or whether it truly identifies a dopaminergic asymmetry related to the disease process, as Bracha's results might suggest.

The other major subgroup of dopamine receptors has received far less attention, although there is an increasing interest in the potential of drugs acting specifically at D1 receptor sites in the treatment of Parkinsonism and schizophrenia. Thus although they are not thought to be directly involved in the antipsychotic action of neuroleptics, they may modulate D2-related behaviour. An increase in the activation of the second messenger associated with the D1 receptor, adenylate cyclase, has been observed in post-mortem tissue from schizophrenic patients (Memo *et al*, 1983). However, a recent report has described a deficit of about 50% of striatal D1 receptor density (Hess *et al*, 1987), while other groups have been unable to find any difference in this receptor subtype in schizophrenia (Seeman *et al*, 1987; Reynolds & Czudek, 1988). A consistent abnormality of D1 sites in schizophrenia is, therefore, rather unlikely.

Neuropathology of the basal ganglia

Few neuropathological indications of changes in the basal ganglia have been seen in schizophrenia. But while the striatum is not apparently abnormal, the medial part of the globus pallidus has been observed to be decreased in volume by 20% in the Vogt collection of left hemisphere brains (Bogerts *et al*, 1985). Some previous histological studies also showed abnormalities in the pallidum (reviewed by Kleinman *et al*, 1988). These have an interesting parallel in the PET study of Early *et al* (1987), who identified increased cerebral blood flow in the left pallidum of a small series of newly diagnosed unmedicated schizophrenics. As yet our own studies in this region (Reynolds & Czudek, unpublished) have found no post-mortem neurochemical correlate of this lateralised change, although it may conceivably be related to striatal dopamine receptor asymmetry mentioned above.

The limbic brain

A limitation of all the post-mortem studies above is that they concentrate on the striatal regions of the brain which, while they receive the majority of dopaminergic innervation, are primarily concerned with the control of motor function. While there have been attempts to describe how a dysfunction of parts of the striatum may have a fundamental involvement in schizophrenia (e.g. McKenna, 1987), there is little direct support for this view. It is the limbic brain and the cortex which have been particularly associated with the complex behaviour which makes up schizophrenia. These regions of the brain receive dopaminergic innervation from the ventral tegmental area (VTA), a nucleus adjacent to and continuous with the substantia nigra, and it is this mesolimbic dopamine pathway which has, in the past, been particularly implicated in the production of psychosis and antipsychotic drug action (Stevens, 1973; Hornykiewicz, 1978).

There is a wealth of evidence pointing to the pathophysiological involvement of the limbic system and temporal lobe in schizophrenia (Flor-Henry, 1969; Stevens, 1973; Torrey & Peterson, 1974). This derives in part from the association of schizophrenia and schizophreniform psychosis with 'organic' diseases and lesions of the brain (reviewed by Davison, 1987) in which temporal lobe epilepsy (TLE) has perhaps received the most interest. Thus the incidence of schizophrenic psychosis in TLE is approximately 20-fold greater than expected (Ounsted & Lindsay, 1981). Abnormal electrical activity in schizophrenia has been shown in structures of the limbic brain (but not in the striatum) using in-depth electrodes (Heath, 1954), and recurrent electrical stimulation ('kindling') of the VTA has been found to elicit changes in cats which are reminiscent of psychotic behaviour (Stevens & Livermore, 1978). These latter responses are reportedly dependent on intact dopaminergic function.

Limbic dopamine

One limbic structure of the medial temporal lobe which receives a substantial dopaminergic innervation from the VTA is the amygdala, and particularly its central nucleus. However, past neurochemical studies have paid little attention to the amygdala as a potential pathophysiological site in schizophrenia. The first indication of a neurochemical abnormality in this area in schizophrenia was the finding of an increase in the concentration of dopamine in post-mortem brain tissue from two series of patients (Reynolds, 1983). The increase was not reflected by changes in noradrenaline, nor was it observed in the caudate nucleus in the same patients. But, most importantly, it was found to be specific to the left hemisphere, not being found in the right amygdala. This asymmetric increase in amygdala dopamine has been confirmed in a third series, of 19 patients, in whom a corresponding (albeit smaller) asymmetry of HVA, also increased in the left amygdala, was found (Reynolds, 1987). Other neurochemical markers for neurons containing noradrenaline, 5-HT, and acetylcholine have also been investigated, as has the neurotransmitter gamma-aminobutyric acid (GABA), and they show no changes or asymmetry in this region.

While the finding appears to be relatively specific, it is important to note that the results could be due to an effect of neuroleptic treatment, although such a lateralisation of response to drugs would still imply an interesting asymmetry of function in the amygdala. Nor is it clear whether an asymmetry of dopaminergic innervation or of neuronal activity might be responsible for the lateralised increase in amygdala dopamine. The latter interpretation could be a result of unilateral atrophy of another neuronal system which provides a controlling influence on amygdala dopaminergic terminals. Certainly the amygdala receives innervation from a wide range of other brain structures, particularly those of the temporal lobe. What is the evidence for such a deficit of temporal lobe neurons?

Limbic neuropathology

Recent morphological studies of post-mortem brain tissue have yielded strong indications of neuronal deficit which support the view of schizophrenia as a disorder of the limbic brain. These have particularly indicated atrophic abnormalities of temporal lobe structures, including the hippocampus and amygdala, and other related limbic regions. Thus Bogerts *et al* (1985) have studied a small series of left hemispheres taken before the advent of neuroleptic drugs and report a substantial decrease in the size of various limbic structures. In a larger study of 41 carefully selected brains, Brown *et al* (1986) identify a thinning of the parahippocampal gyrus and, along with a recent report (Pakkenberg, 1987), show decreased brain weight and increased ventricular volume. Histological studies also provide evidence for an involvement of certain structures of the limbic system in schizophrenia. A disorganisation of neuronal grouping (Jacob & Beckmann, 1986) and decreased neuronal counts (Falkai *et al*, 1988) in the entorhinal cortex have been observed, as have a disorientation of hippocampal neurons (Kovelman & Scheibel, 1984) and a laminar-specific neuronal loss in frontal and cingulate cortices (Benes *et al*, 1986).

Few neurological investigations have studied both cerebral hemispheres apart from that of Crow and colleagues, who found the parahippocampal gyrus to be relatively thinner in the left hemisphere (Brown *et al*, 1986) and, in their finding that ventricular enlargement was particularly pronounced in the temporal horn of the lateral ventricle in schizophrenia (Crow *et al*, 1988), observed this to be asymmetric with a significantly greater effect in the left hemisphere. Clearly bilateral histological studies are needed to understand the cellular correlates of these asymmetries.

Neurochemical pathology of other limbic transmitter systems

If the observed abnormality in mesolimbic dopamine is related to such atrophy or disorganisation of other neuronal systems within the temporal lobe, then other identifiable neurochemical changes should reflect this more primary disturbance. There is as yet no evidence which relates directly to the dopamine findings, mainly owing to the paucity of bilateral hemispheric studies of post-mortem brain tissue in schizophrenia. However, there are some reported changes involving neuropeptide and amino-acid transmitter systems in the temporal lobe which, along with our understanding of chemical neuroanatomy, certainly provide direction for future study.

The major inhibitory neurotransmitter of the mammalian brain, accounting for perhaps half of all synaptic contacts, is GABA. As well as being present in the neurons of the striatonigral pathways that are lost in Huntington's disease and which have a reciprocal relationship with the nigrostriatal dopaminergic system, GABA is also found in a large proportion of cortical interneurons, cells which several of the above histological studies implicate in schizophrenia. A reduced activity of this neurotransmitter has long been hypothesised as an aetiological factor in schizophrenia (Roberts, 1972). This followed from observation of the close association between dopamine and GABA systems (at least in the basal ganglia) and potentially provided rationale for a relative enhancement of dopaminergic activity in the disease. So far, however, there has been no post-mortem evidence to support the hypothesis. An initial finding of decreased activity of glutamate decarboxylase (the GABA-synthesising enzyme) was subsequently found to be an artefact of agonal state differences (Bird *et al*, 1978). Concentrations of GABA have also been found to be normal in several areas (Cross *et al*, 1979) including the amygdala (Reynolds, 1986).

However, GABA systems have been under-investigated in the limbic brain in schizophrenia. Most of these previous studies have concentrated on the basal ganglia, since it is these regions in which the reciprocal relationship between GABA and the nigrostriatal dopaminergic system is best understood. Nothing is known of the effect, if any, that a deficit in GABA might have on mesolimbic or mesocortical dopamine function. Nevertheless, there are other neurochemical observations which are rather more consistent with a limbic neuronal loss in schizophrenia and which provide a hint of the possible involvement of GABA systems.

Changes in the concentrations of several neuropeptides in temporal lobe structures have been reported. While Kleinman *et al* (1983) observed no abnormality in the content of cholecystokinin (CCK) in a range of limbic, cortical, and basal ganglia regions in schizophrenia, this peptide has been found to be reduced in the hippocampus and amygdala of patients presenting with negative symptoms, as was hippocampal somatostatin content (Ferrier *et al*, 1983; Roberts *et al*, 1983). Further evidence implicating a chemical neuropathology of CCK in schizophrenia is the observation of losses of CCK binding sites, presumed to be receptors, in the hippocampus (Farmery *et al*, 1985). Neurotensin has been implicated in psychosis and antipsychotic drug action, particularly via its interaction with dopamine systems, but from several studies there has been no reliable indication of an abnormality of neurotensin concentrations in the brain in schizophrenia (Bissette *et al*, 1986).

Of the investigations into neuropeptide changes in schizophrenia, not one has attempted either to identify lateral hemispheric asymmetries or determine their relationship to neuropathological changes. But those changes mentioned above that are associated with previous negative symptoms in the patients studied, which in turn may relate to ventricular enlargement (Andreasen *et al*, 1982), do provide a potential correlate with neuropathology. The CCK results are especially notable in this respect, since the peptide is found to coexist with dopamine in certain mesolimbic neurons (Hokfelt *et al*, 1980). However, the opposite direction of the changes observed for these two transmitters in schizophrenia suggests the possible involvement of another neuronal group. CCK in the (cat) cortex and hippocampus is thought to be almost exclusively contained within GABAergic neurons (Somogyi *et al*, 1984), again indicating the involvement of this amino-acid transmitter.

The influence of CCK on dopamine systems in the limbic brain has received some study. Suggestions have emerged that CCK and related peptides act via an inhibition of limbic dopaminergic activity, with behavioural effects following intracerebral injection in the rat that resemble those of the neuroleptic drugs (van Ree *et al*, 1983). Thus a disturbance of CCK-containing neurons could well lead to a hyperactivity of limbic dopamine systems. There have also been occasional reports that CCK-related peptides have proved effective in treating some schizophrenic patients, athough a recent review (Montgomery & Green, 1988) found that too few adequately controlled studies had been undertaken to draw valid conclusions.

The known interaction of CCK with dopamine systems has been reviewed by Roberts (1989) who has taken this evidence, along with the recent neuropathological findings, to construct a valuable hypothesis for the developmental aetiology of schizophrenia. This builds on the indications that CCK may have a neurotrophic role in the developing brain, and concludes that a disruption of CCK systems may well result in the neuropathology, both chemical and morphological, that is presently apparent in the brain in schizophrenia. While it is outside the scope of this review to discuss potential aetiology in any detail, it is worth commenting that the involvement of such a trophic factor does provide for a common mechanism whereby both genetic factors and development disturbance can lead to neuronal dystrophy, or apparent atrophy.

Most recently, neurochemical evidence for a lateralised neuronal dysfunction in schizophrenia has emerged. A study of glutamate receptor sites in the hippocampus has demonstrated a deficit in binding to a kainate-sensitive subgroup of these receptors, an effect which is found in the left hemisphere in the schizophrenic group (Kerwin *et al*, 1988). Although this has not been confirmed by Deakin *et al* (1989), the latter group used substantially different conditions. The result is perhaps most easily interpreted in terms of loss of post-synaptic neurons, and is certainly compatible with the proposed 'glutamate hypothesis' of schizophrenia (Kim *et al*, 1980), despite the lack of evidence for decreased pre-synaptic glutamatergic function.

The frontal cortex

Thus neurochemical evidence, along with neuropathological, behavioural, and physiological indications, support the view that a (possibly lateralised) dysfunction within the temporal/limbic structures of the brain might be responsible for the symptoms of schizophrenia. However, other areas of the cortex have been especially implicated. The evidence for this (reviewed by Weinberger, 1987) is partly from psychological/behavioural studies, from tomographic imaging observations, and from neuropharmacological experiments.

Brain imaging has particularly focused on the frontal cortex. Since first being described by Ingvar & Franzen (1974), a relative decrease in frontal cortical blood flow in some schizophrenic patients has been observed repeatedly, although not invariably. PET has also been used to measure energy metabolism and this too has occasionally, if inconsistently, shown evidence of hypofrontality (Weinberger & Berman, 1988). In several studies, hypofrontality was found to correlate with various more negative symptoms (Ingvar, 1987), providing a parallel with the relationships between cortical atrophy and symptoms suggested by imaging and CSF biochemistry. However, the evidence has led Weinberger (1988) to conclude that these changes are in part a consequence of pathology of temporal limbic structures.

Dopamine and the frontal cortex

Another major reason for the development of the theory of schizophrenia as a disorder of the frontal cortex is that it is considered to be consistent with the 'dopamine hypothesis'. In the rodent, at least, there is a substantial dopaminergic innervation of the frontal cortex but not of other neocortical regions (Bannon & Roth, 1983). Although in man cortical dopaminergic innervation is both more generalised and far less dense, it has been suggested that this system mediates the effects of antipsychotic drugs. The apparent lack of autoreceptors on the dopamine neuronal terminals in this region is held responsible for the unique response to chronic neuroleptic administration; an initial increase in dopamine metabolites subsequently diminishes in most brain regions as autoreceptor-mediated inhibition of dopamine synthesis occurs, although this tolerance does not develop in the frontal cortex (Bannon &

Roth, 1983). This effect may also occur in man and implicates the cortex in antipsychotic mechanisms. But no inherent neurotransmitter change has yet been identified which might correlate with a primary cortical dysfunction in schizophrenia.

Nevertheless, there remains a strong interest in the possibility that a lesion in the frontal cortex may induce an increase in dopaminergic activity in subcortical brain regions. This proposal follows from an experiment by Pycock *et al* (1980) in which the effects of frontal cortical 6-hydroxydopamine lesions in rats were studied. The lesions resulted in increased striatal and limbic dopamine metabolism and receptor density. This presumably reflected regulatory feedback from the cortex to subcortical dopamine sites and, while this corticolimbic pathway has yet to be identified (Christie *et al*, 1986), it provided a hypothesis for integrating evidence for frontal cortical damage with an increase in subcortical dopamine function in schizophrenia. However, since dopamine receptor increases in the striatum are likely to be drug-induced, and the changes in limbic dopamine are highly specific, the value of this theory is now very limited. The most damning evidence is that there is an increase (albeit probably drug-induced) of dopamine metabolism in the cortex in schizophrenia, as indicated by increased concentrations of HVA in post-mortem studies (Bacopoulos *et al*, 1979*b*; Reynolds & Czudek, 1988), and no direct evidence whatsoever of frontal dopaminergic damage.

Neurochemical pathology of the frontal cortex

However, other neurochemical findings do indicate frontal cortical abnormalities. These involve the post-synaptic receptors that mediate glutamate neurotransmission, particularly the subtype defined by the kainate binding site. Nishikawa *et al* (1983) have reported an increase in kainate binding in the medial pre-frontal cortex in schizophrenia which was not observed in other frontal (including orbital) cortical areas, nor in the putamen. A similar increase has been shown by Deakin *et al* (1989) to occur, not in the medial frontal, but in the orbital cortex. They also show an increase in the membrane binding of D-aspartate to this region of the frontal cortex. D-aspartate binds to the glutamate uptake site and so provides a marker for the density of glutamatergic terminals. One further receptor type is thought to be changed in this brain region in schizophrenia. As they found in the hippocampus, Farmery *et al* (1985) reported a deficit of CCK binding sites in frontal cortex.

It is unclear how these various changes (which are mostly unconfirmed single studies) can, if they prove to be repeatable and representative, be reconciled with one another. Decreased receptor density is most easily explained by loss of the neurons on which those receptors are found. Increases, however, may relate to either 'up-regulation' (due to decreased synaptic activity) or abnormally high post-synaptic density reflecting an increased innervation or an atrophy in other neuronal systems. If the increased pre- and post-synaptic markers of glutamatergic synapses are indicative of an increased density of excitatory innervation, this is not apparently consistent with the diminished metabolic activity which is described as hypofrontality.

Thus there is clearly a lack of adequate neurochemical study of the frontal cortex and, for that matter, other neocortical areas in schizophrenia, a deficit which is only matched by the paucity of quantitative neuropathological studies. This is in spite of the substantial indications which point to this part of the brain being involved in the symptoms, particularly the negative 'defect state' symptoms, of the disease. One exception is the work of Benes *et al* (1986) who, in a study of these cortical regions, reported that there were neuronal losses, significant in the pre-frontal cortex (area 10), as well as specific laminar deficits in neuronal density which suggest loss of corticofugal pathways. No concomitant increase in glial cells was apparent, suggesting the 'losses' did not reflect a degenerative process but were consistent with a developmental abnormality.

Synthesis

It is not necessarily appropriate to attempt an integration of all this information into a unified theory. Schizophrenia is apparently a collection of syndromes in which one or more of several factors, from the genetic to the traumatic, may be aetiologically important. The clinical appearance too can vary across a wide behavioural spectrum in which there are, admittedly, a few common symptoms. Thus it seems likely that a range of different neuronal abnormalities may be associated with these different causes and manifestations.

In assessing the evidence for a chemical pathology of schizophrenia, it should not be forgotten that the various neurochemical changes in post-mortem brain tissue cannot always be distinguished from the consequences of long-term treatment with antipsychotic drugs. Such drug effects need not only be regulatory responses to, say, dopamine receptor blockade, but may also result from an irreversible neurotoxic action. Such an action on GABAergic neurons of the basal ganglia has been proposed to be responsible for the symptoms of tardive dyskinesia

(Fibiger & Lloyd, 1984), a mainly irreversible side-effect of drug treatment. Both experimental (Gunne *et al*, 1984) and clinical studies (Thaker *et al*, 1987) provide evidence for a loss of GABAergic cells in neuroleptic-induced dyskinesia.

One further complication is provided by the findings mentioned above of pathological (Bogerts *et al*, 1985), and *in vivo* (Early *et al*, 1987), support for neuronal dysfunction in the pallidum of patients who had not received neuroleptic drugs. The pallidum is one region of the brain particularly likely to be involved in the production of abnormal movements. Interestingly, there is a clinical finding consistent with pallidal neuronal disorder. This is the observation that dyskinesias had been reported in schizophrenics before the introduction of the phenothiazines (discussed by Waddington & Crow, 1988), a finding that could indicate an abnormality of basal ganglia systems, and particularly pallidal GABAergic neurons.

Could hippocampal and neocortical neuronal deficits lead to limbic dopaminergic dysfunction?

It would be rash to extrapolate from neurochemical studies into the realms of 'functional neuroanatomy' in order to provide a hypothetical description of how the neuronal changes in various brain regions might result in the behavioural manifestations of schizophrenia. Such a description would inevitably rely on experimental psychology and neuroanatomy in laboratory animals, and its relevance to this very human of diseases would be very questionable. Nevertheless, it is worth re-emphasising that the observed dopaminergic changes in the amygdala do potentially provide a common pathway through which the various neo- and allocortical dysfunctions occurring in schizophrenia might act. The central nucleus of the amygdala is particularly implicated, since this is the region containing the majority of dopaminergic projections to the temporal lobe.

The amygdala is thought to have a role in inter-relating highly processed cortical input and (perhaps thereby) in giving "an affective connotation to the perceptual information" (Gloor, 1986). It is involved in the selection of this sensory information; in this respect it is notable that there has been much discussion as to how the attentional deficits found in schizophrenic patients might relate to a loss of this 'filtering' of information (e.g. Hemsley, 1987).

Certainly there is a substantial innervation of the amygdala by the cortex, although it is true to say that the amygdala both innervates and receives afferents from a large proportion of the structures of the brain. Until we learn the intimate neuronal connections which impinge upon dopamine terminals in the amygdala, we cannot understand how neuronal disturbance in other areas might lead to the changes in amygdalar dopamine. Nevertheless, there is ample room for speculation, some of which could well lead to testable predictions and hypotheses. Thus the central nucleus receives a substantial input from the frontal cortex (e.g. Kapp *et al*, 1985), thereby providing a potential mechanism for the frontal cortical regulation of the amygdala which could lead frontal damage (of whatever aetiology) to induce changes in limbic neurochemistry such as those described above. There is also a major hippocampal input to the central nucleus of the amygdala in the primate; this is primarily excitatory and affects some 20% of the units in this nucleus (Morrison & Poletti, 1980). Thus damage to, say, hippocampal neurons mediating the effects of this pathway could conceivably result in a disinhibition of amygdalar dopamine function. A deficit of the inhibitory interneurons containing GABA, while not directly observed, is implied by the reports mentioned above of decreased concentrations of neuropeptides, several of which are cotransmitters with GABA. Could it be that there is a loss of certain GABA systems in schizophrenia in the hippocampus, parts of the neocortex and/or the pallidum?

Or should we look for a loss of (amygdala) innervation from the excitatory glutamatergic cells of these areas? There is neuropathological evidence in support of both approaches although the diminution of cotransmitter peptides, and unpublished work from the author's laboratory consistent with a loss of GABAergic neuronal terminals in the left hippocampus in schizophrenia, suggests that the first approach might be more fruitful. Furthermore, while it might be presumptuous to describe this collection of loosely related observations as a hypothesis, it does pose some questions. An important one is whether a subtle lesion of hippocampal or cortical GABA (and/or glutamate) neurons leads to increased amygdalar dopamine levels. If so, will this provide a neuroleptic-responsive animal model of psychosis?

While all these speculations are both simplistic and selective, they do provide tentative mechanisms whereby some of the effects of cortical and limbic neuronal deficits, as suggested by neuropathological and neurochemical studies, might be attenuated by neuroleptic drug treatment. They imply, of course, that the dopamine hypothesis no longer provides an indication of the primary abnormality in schizophrenia. And, as has always been true, this hypothesis does not apply to schizophrenia so much as to the 'neuroleptic-responsive psychoses'. It would seem to be less relevant to the treatment-resistant patients who have primarily a negative symptom profile and reportedly more atrophic changes in the brain. One might speculate that these patients have a more generalised cortical neuronal deficit in which an interaction with limbic dopamine systems plays a far smaller part; certainly a greater frontal dysfunction is indicated in these defect state patients.

Thus we are beginning to understand what, and where, neuronal deficits might occur in schizophrenia, and in what directions we should search to learn more. There are many gaps in this picture; one is the absence of adequate (prospective) clinical assessment of patients in most post-mortem neurochemical and pathological studies. This would provide a better comparison with the imaging and biochemical correlates of particular clinical profiles that have been obtained in living patients. Another is the paucity of bilateral observation in these post-mortem investigations; no longer should the neuroscientist assume that the two hemispheres are equivalent. Nevertheless, as we complete our understanding of the neurochemical pathology of schizophrenia, so we shall come closer to the neuronal mechanisms behind the symptoms of the disorder and, thereby, to better approaches to relieving these symptoms in the patient.

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References

Andreasen, N. C., Olsen, S. A., Dennert, J. W., *et al* (1982) Ventricular enlargement in schizophrenia: relationship to positive and negative symptoms. *American Journal of Psychiatry*, **139**, 297–302.

Bacopoulos, N. G., Hattox, S. E. & Roth, R. H. (1979*a*) 3, 4-Dihydroxyphenylacetic acid and homovanillic acid in rat plasma: possible indicators of central dopaminergic activity. *European Journal of Pharmacology*, **56**, 225–236.

——, Spokes, E. G., Bird, E. D., *et al* (1979*b*) Antipsychotic drug action in schizophrenic patients: effects on cortical dopamine metabolism after long-term treatment. *Science*, **205**, 1405–1407.

Bannon, M. J. & Roth, R. H. (1983) Pharmacology of mesocortical dopamine neurons. *Pharmacological Reviews*, **35**, 53–68.

Benes, F. M., Davidson, J. & Bird, E. D. (1986) Quantitative cytoarchitectural studies of the cerebral cortex in schizophrenics. *Archives of General Psychiatry*, **44**, 1017–1021.

Bird, E. D., Spokes, E. G. S., Barnes, J., *et al* (1978) Glutamic acid decarboxylase in schizophrenia. *Lancet*, *ii*, 156.

——, —— & Iversen, L. L. (1979) Increased dopamine concentrations in limbic areas of brain from patients dying with schizophrenia. *Brain*, **102**, 347–360.

Bissette, G., Nemeroff, C. B. & Mackay, A. V. P. (1986) Peptides in schizophrenia. In *Progress in Brain Research*, vol. 66 (eds P. C. Emson, M. Rosser & M. Tohyama). Amsterdam: Elsevier.

Bogerts, B., Meertz, C. & Schonfeldt-Bausch, R. (1985) Basal ganglia and limbic system pathology in schizophrenia: a morphometric study. *Archives of General Psychiatry*, **42**, 784–791.

Bowers, M. B. (1974) Central dopamine turnover in schizophrenic syndromes. *Archives of General Psychiatry*, **31**, 50–54.

—— & Swigar, M. E. (1987) Acute psychosis and plasma catecholamine metabolites. *Archives of General Psychiatry*, **44**, 190.

Bracha, H. S. (1987) Asymmetric rotational (circling) behavior, a dopamine-related asymmetry: preliminary findings in unmedicated and never-medicated schizophrenic patients. *Biological Psychiatry*, **22**, 995–1003.

Brown, R., Colter, N., Corsellis, J. A. N., *et al* (1986) Postmortem evidence of structural brain changes in schizophrenia. *Archives of General Psychiatry*, **43**, 36–42.

Christie, M. J., Rowe, P. J. & Beart, P. M. (1986) Effects of excitotoxic lesions in the medial prefrontal cortex on cortical and subcortical catecholamine turnover in the rat. *Journal of Neurochemistry*, **47**, 1593–1597.

Cleghorn, J. M. & Brown, G. M. (1988) Neuroendocrine studies in schizophrenia. In *Receptors and Ligands in Psychiatry* (eds A. K. Sen & T. Lee). Cambridge: Cambridge University Press.

Clow, A., Theodorou, A., Jenner, P., *et al* (1980) Changes in rat striatal dopamine turnover and receptor activity during one year's neuroleptic administration. *European Journal of Pharmacology*, **63**, 135–144.

Crawley, J. C., Crow, T. J., Johnstone, E. C., *et al* (1986) Dopamine D-2 receptors in schizophrenia studied *in vivo*. *Lancet*, *ii*, 224–225.

Creese, I., Burt, D. R. & Snyder, S. H. (1975) Dopamine receptor binding predicts clinical and pharmacological potencies of antischizophrenic drugs. *Science*, **192**, 481–483.

Cross, A. J., Crow, T. J. & Owen, F. (1979) Gamma-aminobutyric acid in the brain in schizophrenia. *Lancet*, *i*, 560–561.

Crow, T. J., Owen, F., Cross, A. J., *et al* (1981) Neurotransmitter enzymes and receptors in post-mortem brain in schizophrenia; evidence that an increase in D2 receptors is associated with the type I syndrome. In *Transmitter Biochemistry of Human Brain Tissue* (eds P. Riederer & E. Usdin). London: Macmillan.

——, Brown, R., Bruton, C. J., *et al* (1988) Lateral asymmetry of temporal horn enlargement in schizophrenia. *Neuroscience Letters* (suppl. 32), S58.

Czudek, C. & Reynolds, G. P. (1989) [3H]GBR 12935 binding to the dopamine uptake site in post-mortem brain tissue in schizophrenia. *Journal of Neural Transmission* (in press).

Davidson, M., Giordani, A. B., Mohs, R. C., *et al* (1987) Short-term haloperidol administration acutely elevates human plasma homovanillic acid concentration. *Archives of General Psychiatry*, **44**, 189–190.

—— & Davis, K. L. (1988) A comparison of plasma homovanillic acid concentrations in schizophrenic patients and normal controls. *Archives of General Psychiatry*, **45**, 561–563.

Davila, R., Manero, E., Zumarraga, M., *et al* (1988) Plasma homovanillic acid as a predictor of response to neuroleptics. *Archives of General Psychiatry*, **45**, 564–567.

Davis, K. L., Davidson, M., Mohs, R. C., *et al* (1985) Plasma homovanillic acid concentration and the severity of schizophrenic illness. *Science*, **227**, 1601–1602.

Davison, K. (1987) Organic and toxic concomitants of schizophrenia: association or chance? In *Biological Perspectives of Schizophrenia* (eds H. Helmchen & F. A. Henn). Chichester: Wiley.

Deakin, J. F. W., Slater, P., Simpson, M. D. C., *et al* (1989) Frontal cortical and left temporal glutamatergic dysfunction in schizophrenia. *Journal of Neurochemistry*, **52**, 1781–1786.

DeLisi, L. E., Wise, C. D., Bridge, T. P., *et al* (1982) Monoamine oxidase and schizophrenia. In *Biological Markers in Psychiatry and Neurology* (eds E. Usdin & I. Hanin). Oxford: Pergamon.

Doran, A. R., Boronow, J., Weinberger, D. R., *et al* (1987) Structural brain pathology in schizophrenia revisited. *Neuropsychopharmacology*, **1**, 25–32.

Early, T. S., Reiman, E. M., Raichle, M. E., *et al* (1987) Left globus pallidus abnormality in never-mediated patients with schizophrenia. *Proceedings of the National Academy of Sciences (USA)*, **84**, 561–563.

Elsworth, J. D., Leahy, D. J., Roth, R. H., *et al* (1987) Homovanillic acid concentrations in brain, CSF and plasma as indicators of central dopamine function in primates. *Journal of Neural Transmission*, **68**, 51–62.

Falkai, P., Bogerts, B. & Rozumek, M. (1988) Limbic pathology in schizophrenia: the entorhinal region–a morphometric study. *Biological Psychiatry*, **24**, 515–521.

Farde, L., Wiesel, F.-A., Hall, H., *et al* (1987) No D2 receptor increase in PET study of schizophrenia. *Archives of General Psychiatry*, **44**, 671–672.

Farmery, S. M., Owen, F., Poulter, M., *et al* (1985) Reduced high affinity cholecystokinin binding in hippocampus and frontal cortex of schizophrenic patients. *Life Sciences*, **36**, 473–477.

Ferrier, I. N., Roberts, G. W., Crow, T. J., *et al* (1983) Reduced cholecystokinin-like and somatostatin-like immunoreactivity in limbic lobe is associated with negative symptoms in schizophrenia. *Life Sciences*, **33**, 475–482.

Fibiger, H. C. & Lloyd, K. G. (1984) Neurobiological substrates of tardive dyskinesia: the GABA hypothesis. *Trends in Neurosciences*, **7**, 462–464.

Flor-Henry, P. (1969) Psychosis and temporal lobe epilepsy: a controlled investigation. *Epilepsia*, **10**, 363–395.

Gloor, P. (1986) Role of the human limbic system in perception, memory and affect. In *The Limbic System* (eds B. K. Doane & K. E. Livingston). New York: Raven Press.

Gunne, L. M., Haggstrom, J. & Sjoquist, B. (1984) Association with persistent neuroleptic induced dyskinesia of regional changes in brain GABA synthesis. *Nature*, **309**, 347–349.

Heath, R. G. (1954) *Studies in Schizophrenia*. Cambridge: Harvard University Press.

Hemsley, D. R. (1987) An experimental psychological model for schizophrenia. In *Search for the Causes of Schizophrenia* (eds H. Haefner, W. F. Gattaz & W. Janzarik). Heidelberg: Springer.

Hess, E. J., Bracha, H. S., Kleinman, J. E., *et al* (1987) Dopamine receptor subtype imbalance in schizophrenia. *Life Sciences*, **40**, 1487–1497.

Hokfelt, T., Rehfeld, J. F., Skirboll, L., *et al* (1980) Evidence for coexistence of dopamine and CCK in mesolimbic neurons. *Nature*, **285**, 476–478.

Hornykiewicz, O. (1978) Psychopharmacological implications of dopamine and dopamine antagonists. *Neuroscience*, **3**, 773–783.

Ingvar, D. H. (1987) Evidence for frontal/prefrontal cortical dysfunction in chronic schizophrenia: the phenomenon of "hypofrontality" reconsidered. In *Biological Perspectives of Schizophrenia* (eds H. Helmchen & F. A. Henn). Chichester: Wiley.

—— & Franzen, G. (1974) Abnormalities of cerebral blood flow distribution in patients with chronic schizophrenia. *Acta Psychiatrica Scandinavica*, **50**, 425–436.

Jacob, H. & Beckmann, H. (1986) Prenatal development disturbances in the limbic allocortex in schizophrenics. *Journal of Neural Transmission*, **65**, 303–326.

Kaff, B. S., Schwaber, J. S. & Driscoll, P. A. (1985) Frontal cortex projections to the amygdaloid central nucleus in the rabbit. *Neuroscience*, **15**, 327–346.

Kerwin, R. W., Patel, S., Meldrum, B. S., *et al* (1988) Asymmetrical loss of glutamate receptor subtype in left hippocampus in schizophrenia. *Lancet*, *i*, 583–584.

Kim, J. S., Kornhuber, J. J., Schmid-Burgk, W., *et al* (1989) Low cerebrospinal fluid glutamate in schizophrenic patients and a new hypothesis on schizophrenia. *Neuroscience Letters*, **20**, 379–382.

Kleinman, J. E., Iadarola, M., Govoni, S., *et al* (1983) Postmortem measurements of neuropeptides in human brain. *Psychopharmacology Bulletin*, **19**, 375–377.

——, Casanova, M. F. & Jaskiw, G. E. (1988) The neuropathology of schizophrenia. *Schizophrenia Bulletin*, **14**, 209–216.

Kovelman, J. A. & Scheibel, A. B. (1984) A neurohistological correlate of schizophrenia. *Biological Psychiatry*, **19**, 1601–1621.

Lee, T., Seeman, P., Tourtellotte, W. W., *et al* (1978) Binding of ^{3}H-neuroleptics and ^{3}H-apomorphine in schizophrenic brains. *Nature*, **274**, 897–900.

Losonczy, M. F., Song, I. S., Mohs, R. C., *et al* (1986) Correlates of lateral ventricle size in chronic schizophrenia. II: biological correlates. *American Journal of Psychiatry*, **143**, 1113–1118.

Mackay, A. V. P., Iversen, L. L., Rossor, M., *et al* (1982) Increased brain dopamine and dopamine receptors in schizophrenia. *Archives of General Psychiatry*, **39**, 991–997.

McKenna, P. J. (1987) Pathology, phenomenology and the dopamine hypothesis of schizophrenia. *British Journal of Psychiatry*, **151**, 288–301.

Memo, M., Kleinman, J. E. & Hanbauer, I. (1983) Coupling of dopamine D1 recognition sites with adenylate cyclase in nuclei accumbens and caudatus of schizophrenia. *Science*, **221**, 1304–1307.

Montgomery, S. A. & Green, M. C. D. (1988) The use of cholecystokinin in schizophrenia: a review. *Psychological Medicine*, **18**, 593–603.

Morrison, F. & Poletti, C. E. (1980) Hippocampal influence on amygdala unit activity in awake squirrel monkeys. *Brain Research*, **192**, 353–369.

Nishikawa, T., Takashima, M. & Toru, M. (1983) Increased (3H)kainic acid binding in the prefrontal cortex in schizophrenia. *Neuroscience Letters*, **40**, 245–250.

Ounsted, C. & Lindsay, J. (1981) In: *Epilepsy and Psychiatry* (eds E. H. Reynolds & M. R. Trimble). Edinburgh: Churchill Livingstone.

Owen, F., Crow, T. J., Poulter, M., *et al* (1978) Increased dopamine-receptor sensitivity in schizophrenia. *Lancet*, *ii*, 223–225.

—— & —— (1987) Neurotransmitters and psychosis. *British Medical Bulletin*, **43**, 651–671.

Pakkenberg, B. (1987) Post-mortem study of chronic schizophrenic brains. *British Journal of Psychiatry*, **151**, 744–752.

Pickar, D., Labarca, R., Linnoila, M., *et al* (1984) Neuroleptic-induced decrease in plasma homovanillic acid and antipsychotic activity in schizophrenic patients. *Science*, **225**, 954–957.

——, ——, Doran, A. R., *et al* (1986) Longitudinal measurement of plasma homovanillic acid levels in schizophrenic patients. *Archives of General Psychiatry*, **43**, 669–676.

Potkin, S. G., Weinberger, D. R., Linnoila, M., *et al* (1983) Low CSF 5-hydroxyindoleacetic acid in schizophrenic patients with enlarged ventricles. *American Journal of Psychiatry*, **140**, 21–25.

Pycock, C. J., Kerwin, R. W. & Carter, C. J. (1980) Effect of lesion of cortical dopamine terminals on subcortical dopamine receptors in rats. *Nature*, **286**, 74–77.

Randrup, A. & Munkvad, I. (1965) Special antagonism of amphetamine-induced abnormal behaviour. *Psychopharmacologia*, **7**, 416–422.

Reynolds, G. P. (1983) Increased concentrations and lateral asymmetry of amygdala dopamine in schizophrenia. *Nature*, **305**, 527–529.

—— (1986) Amygdala dopamine asymmetry in schizophrenia: neurochemical evidence for a left temporal lobe dysfunction. In *Dopaminergic Systems and Their Regulation* (eds G. N. Woodruff, J. A. Poat & P. J. Roberts). London: Macmillan.

—— (1987) Post-mortem neurochemical studies in schizophrenia. In *Search for the Causes of Schizophrenia* (eds H. Haefner, W. F. Gattaz & W. Janzarik). Heidelberg: Springer.

—— (1988) Post-mortem neurochemistry of schizophrenia. *Psychological Medicine*, **18**, 793–797.

——, Riederer, P., Jellinger, K., *et al* (1981) Dopamine receptors and schizophrenia: the neuroleptic drug problem. *Neuropharmacology*, **20**, 1319–1320.

——, Czudek, C., Bzowej, N., *et al* (1987) Dopamine receptor asymmetry in schizophrenia. *Lancet*, *i*, 979.

—— & —— (1988) Status of the dopaminergic system in post-mortem brain in schizophrenia. *Psychopharmacology Bulletin*, **24**, 345–347.

Roberts, E. (1972) An hypothesis suggesting that there is a deficit in the GABA system in schizophrenia. *Neuroscience Research Program Bulletin*, **10**, 468–481.

Roberts, G. W. (1989) Brain development and CCK systems in schizophrenia: a working hypothesis. In *Advances in Biological Psychiatry* (ed. M. P. O. Weller). London: Libbey (in press).

——, Ferrier, I. N., Lee, Y., *et al* (1983) Peptides, the limbic lobe and schizophrenia. *Brain Research*, **288**, 199–211.

Seeman, P., Lee, T., Chau-Wong, M., *et al* (1976) Antipsychotic drug doses and neuroleptic/dopamine receptors. *Nature*, **261**, 717–719.

——, Ulpian, C., Bergeron, C., *et al* (1984) Bimodal distribution of dopamine receptor densities in brains of schizophrenics. *Science*, **225**, 728–731.

——, Bzowej, N. H., Guan, H. C., *et al* (1987) Human brain D1 and D2 dopamine receptors in schizophrenia, Alzheimer's, Parkinson's and Huntington's diseases. *Neuropsychopharmacology*, **1**, 5–15.

Snyder, S. H., Banerjee, S. P., Yamamura, H. T., *et al* (1974) Drugs, neurotransmitters and schizophrenia. *Science*, **184**, 1243–1253.

Somogyi, P., Hodgson, A. J., Smith, A. D., *et al* (1984) Different populations of GABAergic neurons in the visual cortex and hippocampus of cat contain somatostatin- or cholecystokinin-immunoreactive material. *Journal of Neuroscience*, 4, 2590–2603.

Stanley, M., Traskman-Bendz, L. & Dorovini-Zis, K. (1985) Correlations between aminergic metabolites simultaneously obtained from human CSF and brain. *Life Sciences*, **37**, 1279–1286.

Stevens, J. R. (1973) An anatomy of schizophrenia? *Archives of General Psychiatry*, **29**, 177–189.

—— & Livermore, A. (1978) Kindling of the mesolimbic dopamine systems. Animal model of psychosis. *Neurology*, **28**, 36–46.

Thaker, G. K., Tamminga, C. A., Alphs, L. D., *et al* (1987) Brain γ-aminobutyric acid abnormality in tardive dyskinesia. *Archives of General Psychiatry*, **44**, 522–529.

Torrey, E. F. & Peterson, M. R. (1974) Schizophrenia and the limbic system. *Lancet*, *ii*, 942–946.

Tyrer, P. & Mackay, A. (1986) Schizophrenia: no longer a functional psychosis. *Trends in Neurosciences*, **9**, 537–538.

Van Kammen, D. P., Mann, L. S., Sternberg, D. E., *et al* (1983) Dopamine-β-hydroxylase activity and homovanillic acid in spinal fluid of schizophrenic with brain atrophy. *Science*, **220**, 974–977.

Van Ree, J. M., Gaffori, O. & De Wied, D. (1983) In rats the behavioural profile of CCK-8 related peptides resembles that of antipsychotic agents. *European Journal of Pharmacology*, **93**, 63–78.

Waddington, J. L. (1989) Sight and insight: brain dopamine receptor occupancy by neuroleptics visualised in living schizophrenic patients by positron emission tomography. *British Journal of Psychiatry*, **154**, 433–436.

—— & Crow, T. J. (1988) Abnormal involuntary movements and psychosis in the pre-neuroleptic era and in unmedicated patients: implications for the concept of tardive dyskinesia. In *Tardive Dyskinesia: Biological Mechanisms and Clinical Aspects* (eds M. E. Wolf & A. D. Mosnaim). Washington, DC: American Psychiatric Press.

Weinberger, D. R. (1987) Implication of normal brain development for the pathogenesis of schizophrenia. *Archives of General Psychiatry*, **44**, 660–669.

—— (1988) Schizophrenia and the frontal lobe. *Trends in Neurosciences*, **11**, 367–370.

—— & Berman, K. F. (1988) Speculation on the meaning of cerebral metabolic hypofrontality in schizophrenia. *Schizophrenia Bulletin*, **14**, 157–168.

Wong, D. F., Wagner, H. N., Tune, L. E., *et al* (1986) Positron emission tomography reveals elevated D-2 dopamine receptors in drug-naive schizophrenics. *Science*, **234**, 1558–1563.

Zeeberg, B. R., Gibson, R. E. & Reba, R. C. (1988) Elevated D2 dopamine receptors in drug naive schizophrenics. *Science*, **239**, 789–790.

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The Guy's/Age Concern Survey
Prevalence Rates of Cognitive Impairment, Depression and Anxiety in an Urban Elderly Community

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A sample of 890 people aged 65 years and over living at home in the Lewisham and North Southwark Health District was interviewed using a structured schedule containing CARE organic brain syndrome and depression scales, and items dealing with anxiety symptoms. Total prevalence rates were 4.6% for cognitive impairment, 13.5% for depression, 3.7% for generalised anxiety; and 10.0% for phobic disorders. Cognitive impairment increased exponentially with age, and was associated with lower occupational class. There was no significant association between occupational class and depression, generalised anxiety, or phobic disorder in this sample. Cognitive impairment, depression and agoraphobia were associated with significantly higher levels of dependency in the tasks of daily living.

The growing number of people aged 65 years and over in developed countries is presenting a major challenge to their health and social services. As a result of this 'demographic imperative', service planners are now examining how the limited resources available are to be used cost-effectively to provide an acceptable standard of treatment and care for this age group. In the elderly, mental disorder is a key factor affecting the use of acute hospital beds; the need for residential care and the demand upon domiciliary services. Conditions such as dementia, depression and anxiety influence decisions as to whether or not physical illness can be managed at home; they determine the capacity for self-care and the ability to perform the daily tasks of life; and, because of the practical and emotional burden imposed upon the family and neighbours, they may lead to institutionalisation or heavy investment in domiciliary services.

Epidemiological investigations of mental disorders in the elderly therefore have an important role in providing accurate and up-to-date information for planners (Henderson & Macfadyen, 1985). However, only a small proportion of the published studies provide data that are sufficiently reliable, detailed or comprehensive for planning purposes. In particular, information about the very old (over 75 years of age) is often not reported separately, or else is derived from small subsamples of the over-65s, as Morgan *et al* (1987) have pointed out.

Furthermore, few studies have looked at a broad range of mental disorders in the elderly. Cognitive impairment and depression have been extensively surveyed, but there is much less information available about other disorders, particularly anxiety states, in spite of the fact that they appear to be relatively common in old age. In the multi-centre Epidemiological Catchment Area (ECA) study in the United States, phobias were found to be the commonest disorder in women aged 65 and over, and the second commonest after cognitive impairment in men of this age (Myers *et al*, 1984). It is not known how disabling or distressing anxiety disorders are in old age, but their clinical importance may be judged from the fact that the elderly are among the heaviest consumers of anxiolytic drugs (Skegg *et al*, 1977; Catalan *et al*, 1988).

In 1986 the Section of Psychogeriatrics in the United Medical and Dental Schools (Guy's Campus), in conjunction with the Age Concern Institute of Gerontology, carried out a survey of the health and self-care capacity of elderly people living at home in the Lewisham and North Southwark Health District. The specific aims of this project were to establish for this population: the prevalence of cognitive impairment, depression and anxiety disorders; the nature and extent of physical health problems; levels of dependency and self-care capacity; and the utilisation and targetting of health and social services in this population. This paper reports the prevalence rates of cognitive impairment, depression and anxiety disorders estimated in this survey.

Method

The sample

The survey was conducted in the Lewisham and North Southwark Health District. This is a typical socially deprived segment of inner-city London; according to the Inner City Directorate of the Department of the

Environment, on the basis of indicators derived from the 1981 Census data, Southwark is the tenth most deprived local authority in Greater London, and Lewisham is the twelfth. The elderly population of the district tend to be poor, and more socially isolated than those elderly living outside London. They are almost all white, born in the UK or Europe, and most have lived in the district for the major part of their lives.

At the 1981 Census the total population resident in the district was 311 959, including 50 241 (16.1%) aged 65 years and over. Of these, 19 147 (38.1%) were aged 75 years and over. For this survey the Electoral Register was chosen as the best sample frame available in the district. The projected sample size for the survey was approximately 1000 elderly subjects, so an initial random sample of 6178 names was drawn from the register. These individuals were screened by post to determine their date of birth. In order to maximise response to the postal screen, this enquiry was put in the context of a brief health questionnaire (Cartwright & Smith, 1987). Non-responders to this screen were sent a reminder, and non-responders to the reminder were followed up personally by the interviewers as part of the survey.

Most elderly people are included in the Electoral Register (Todd & Butcher, 1982), but boroughs vary in their methods of registering electors, and in some areas those with cognitive impairment might be at risk of dropping out or being excluded. The extent to which subjects with dementia were missing from the survey sample frame was estimated as follows. The names and addresses of the 101 patients presenting to an open-referral psychogeriatric community team in Lewisham in 1986 who received a clinical diagnosis of dementia were sought in the borough's Electoral Register for 1986 (qualifying date for entry 10 October 1985). Of those living at home at the time of referral, 83/88 (94%) were present in the register.

Instruments

The interview schedule consisted of structured questions and tests dealing with social and demographic factors, physical and mental health status, self-care capacity, dependency and utilisation of health and social services. Cognitive impairment and depression were assessed with slightly modified versions of the organic brain syndrome (OBS) and depression (D) scales of the CARE schedule, which have been extensively validated in community samples of the elderly by trained non-medical interviewers (Gurland *et al*, 1977; Gurland *et al*, 1984).

No equivalent means of detecting anxiety disorders in the elderly was available at the time of the survey, so a generalised anxiety (GA) scale was constructed for this survey, covering the areas of motor tension, autonomic hyperactivity, apprehensive expectation and hyper-vigilance. Where possible, items from existing scales were used or adapted, in particular the CARE schedule, the Present State Examination (PSE) (Wing *et al*, 1974) and the Geriatric Mental State (GMS) (Copeland *et al*, 1976) (Appendix 1). The interview schedule also contained items dealing with situational and specific fears. If any fears were present, subjects were asked about associated autonomic symptoms and phobic avoidance, and whether or not this was perceived by the subject as restricting (Appendix 1). No prior assumptions were made about what fears might be reasonable or unreasonable in this age group, and phobic disorders (Ph) were defined categorically as agoraphobic, social or specific fears with autonomic symptoms accompanying exposure to the phobic stimulus, or associated with restricting secondary avoidance. Panic attacks were rated separately, and panic disorder (PD) was defined according to DSM–III criteria (American Psychiatric Association, 1980). Post-traumatic stress disorder and obsessive–compulsive disorder were not rated in this survey.

The OBS scale consisted of test items, so it yielded a point prevalence of cognitive impairment. The D, GA, Ph and PD items were rated on the subjects' reported experiences in the month prior to interview, giving one-month prevalence rates for depression and anxiety disorders in this survey.

Validity and reliability

The validity and inter-rater reliability of the scales were assessed as part of the survey. Two validation exercises were carried out: a pre-survey pilot study of the schedule and a reinterview of a group of survey subjects. In the pilot study 21 elderly subjects were first interviewed by a member of the research team, using a schedule containing the OBS, D, GA, Ph and PD items, and then reinterviewed blind by a psychiatrist, using the PSE. None of these pilot subjects was subsequently included in the survey sample. In the survey validation, 33 subjects were reinterviewed blind by a psychiatrist, using the PSE.

The validity criteria were as follows: for the D scale a psychiatrist's clinical diagnosis of depression supported by a CATEGO-derived Index of Definition (ID) of 4 or more (Wing, 1976); for the GA scale a clinical diagnosis of generalised anxiety and an ID of 4 or more; for the Ph scale a clinical diagnosis of a phobic disorder and an ID of 4 or more; for the PD scale a clinical diagnosis of panic disorder and an ID of 4 or more; and for the OBS scale a clinical diagnosis of cognitive impairment alone. An ID of 5 or more implies that sufficient PSE symptoms are present for the CATEGO program to assign an ICD–8 diagnosis (Wing, 1976); an ID of 4 implies that specific symptoms are present, and is usually taken as the threshold between non-cases (ID 0–3) and cases. A higher cut-off point on the D scale was also validated against a clinical diagnosis of depression and an ID of 5 or more.

The relationship between these definitions of psychiatric disorder and functional impairment was estimated by a dependency scale of 13 self-report items concerned with self-care and domestic tasks derived from those used by Hunt (1978) (Appendix 2). Informant-rated scales of dependency were not used, since a substantial minority of elderly householders live alone. Where an informant was present, their observations were taken into account when rating these items. The internal consistency of the dependency scale was measured by Cronbach's α.

TABLE I

Demographic characteristics of the sample compared with the total elderly population of Lewisham and North Southwark (1981 Census)

	Survey %	*1981 Census* %
North Southwark	26.6	27.9
Lewisham	73.4	72.1
Men	40.1	38.0
Women	59.9	62.0
Age 65–74	60.9	61.3
75–84	31.2	30.9
85+	7.9	7.8
Married	48.9	52.6
Non-married	51.1	47.4

TABLE II

Distribution of the sample classified according to age and sex

	Men	*Women*	*Total*
65–74	250 (28.0%)	292 (32.8%)	542 (60.9%)
75–84	92 (10.3%)	186 (20.9%)	278 (31.2%)
85+	15 (1.7%)	55 (6.2%)	70 (7.9%)
Total	357 (40.1%)	533 (59.9%)	890 (100%)

TABLE III

Validation coefficients for the organic brain syndrome (OBS), depression (D), generalised anxiety (GA) and phobia (Ph) scales

Scale *cut-off point*	*OBS* *2/3* %	*D* *7/8* %	*D* *12/13* %	*GA* *4/5* %	*Ph* *−/+* %
Specificity	98	90	98	98	93
Sensitivity	75	92	69	71	73
Positive predictive value	75	76	90	83	73
Misclassification rate	4	9	9	6	11

Procedure

Interviews were carried out between January and October 1986 by seven non-medical interviewers recruited for this survey (three men and four women). The interviewers were trained in the use of the interview schedule, in particular the OBS, D, GA, Ph and PD items. Before the survey proper, each interviewer completed a number of supervised and co-rated field interviews. The interviewers were also given a reference manual setting out coding instructions for the schedule items for use during the survey period. The mean duration of the survey interviews was 1 hour and 16 minutes (standard deviation ± 37 minutes).

The survey data were analysed by the Statistical Package for the Social Sciences (10th edn) (1986). All χ^2 tests include Yates' correction. Significant differences in dependency scores between groups were tested by the Mann–Whitney *U*-test, corrected for ties.

Results

The sample

Of 1113 individuals identified as born before 1921, 1030 were eligible for inclusion in the survey. Thirty had died, and the 53 ineligible subjects were those who had moved out of the district, or who were in residential care. Forty-seven subjects were not contacted. Of 983 individuals contacted, 892 were interviewed for the main survey (91 refused) and 890 interviews were completed, giving a response rate of 86% of those eligible.

The socio-demographic characteristics of the survey sample were comparable with those of the elderly population of the district in general, as given by the 1981 Census (Table I). The distribution of the sample classified according to age and sex matches that of the district population as a whole (Table II), so the prevalence estimates reported here are unweighted.

Validity and reliability

The results of the two validation exercises were similar, and the coefficients at the optimum cut-off points for both groups combined ($n=54$) are given in Table III. These optimum cut-off points were: 2/3 for the OBS scale, 7/8 (ID 4+) and 12/13 (ID 5+) for the D scale and 4/5 for the GA scale. No cases of panic disorder were identified by either interviewers or psychiatrists in the validation samples.

The interviewers' inter-rater reliability, assessed by weighted κ, was 0.82 for the OBS scale, 0.90 for the D scale and 0.87 for the GA scale. For phobic disorders (Ph), assessed by Cohen's κ, the inter-rater reliability was 1.0 (no disagreements).

The reliability of the dependency scale in terms of its internal consistency (Cronbach's α) was 0.72. The interviewers' inter-rater reliability for this scale (weighted κ) was 0.90.

Cognitive impairment

Table IV shows the prevalence rates of cognitive impairment classified according to sex and age of subject. The rates of broad (OBS 3+) and narrow (OBS 6+) definitions of cognitive impairment were higher in women. The difference in the proportion of cases to non-cases for men and women was not significant at the 0.05 level, but a one-way analysis of variance of OBS score by gender did show a significant difference between scores for men and women (Kruskall–Wallis $H=6.8$; $P<0.01$). Of the men with OBS scores of 3 or more 28.6% were aged 65–74, compared with 18.5% of women with OBS 3+ scores.

TABLE IV
Point prevalence rates (%) of cognitive impairment (OBS), classified according to sex and age of subject[1]

OBS score %	*Men*			*Women*			*Total*
	65–74	*75+*	*Total men*	*65–74*	*75+*	*Total women*	
3+	1.6 (±1.5)	9.3 (±5.6)	3.9 (±2.0)	1.7 (±1.5)	9.1 (±3.6)	5.1 (±1.9)	4.6 (±1.4)
4+	1.2 (±1.4)	3.7 (±3.6)	2.0 (±1.4)	1.4 (±1.3)	7.1 (±3.2)	3.9 (±1.7)	3.1 (±1.1)
6+	0.4 (±0.8)	1.9 (±2.6)	0.8 (±0.9)	0.3 (±0.7)	2.5 (±2.0)	1.3 (±1.0)	1.1 (±0.7)

1. Figures in parentheses give 95% confidence intervals.

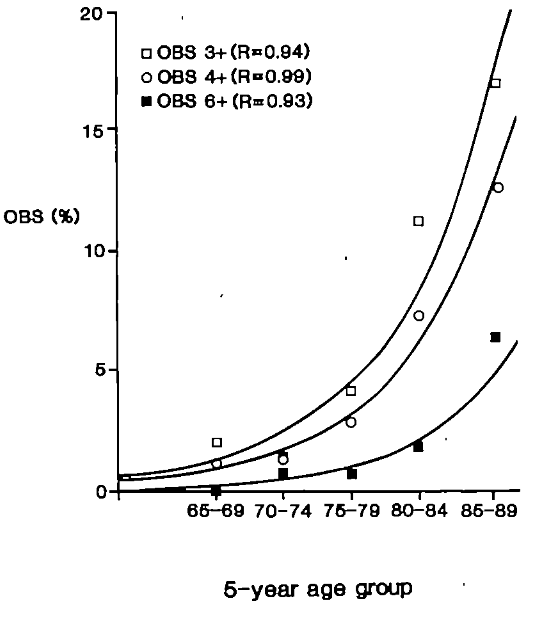

FIG. 1 Prevalence of three severities of cognitive impairment (OBS) for five-year age groups, with best-fit exponential plots.

In order to examine the association between age and the prevalence of cognitive impairment, rates for the five 5-year age groups from 65–69 years to 80–89 years were calculated for OBS cut-off points 3+ (mild–severe cases), 4+ (moderate–severe cases) and 6+ (severe cases only), and plotted against the median age of each age group (Fig. 1). At each cut-off point the increasing prevalence with age closely followed an exponential curve, with a doubling of the rate every 4.7–5.6 years (mean period = 5.3 years). The total number of subjects in the 5-year groups aged 90 and over was very small ($n = 22$), and the prevalence rates of cognitive impairment have very wide 95% confidence intervals (OBS 3+: 23% ± 19%; OBS 6+: 9% ± 13%). They have therefore been excluded from this analysis.

Table V gives the rates of cognitive impairment for different social classes in the sample, classified according to the Office of Population Censuses and Surveys (OPCS) classification of occupations (1970). The occupation determining social class was the last before retirement in all cases, either the subject's own in the case of men and single women or the spouse's for married and widowed women. There was a significant difference in rates between classes ($\chi^2 = 9.42$; $P < 0.05$; d.f. = 3), with higher rates in lower classes. This difference remained significant if non-single female subjects were classified according to their own rather than their spouses' previous occupations ($\chi^2 = 7.86$; $P < 0.05$; d.f. = 3).

Subjects with an OBS score of 3+ had significantly higher dependency scores than those with an OBS score of 0–2 ($z = 7.84$; two-tailed $P < 0.0001$) (Table VI). There was also a significant correlation between the OBS and dependency scores in this sample ($r = 0.38$; one-tailed

TABLE V
Prevalence rates of cognitive impairment, depression and anxiety disorders classified according to social class of subject

Class	*Total*	*OBS 3+*	*D 8+*	*D 13+*	*GA 5+*	*Ph+*
I/II	3	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
III N	157	2 (1.3%)	21 (13.4%)	10 (6.4%)	5 (3.2%)	17 (10.8%)
III M	455	18 (4.0%)	70 (15.4%)	22 (4.8%)	18 (3.9%)	48 (10.5%)
IV/V	219	16 (7.3%)	22 (10.0%)	9 (4.1%)	9 (4.1%)	21 (9.6%)
Other/?	56	5 (8.9%)	7 (12.5%)	3 (5.3%)	1 (1.8%)	3 (5.3%)

$P < 0.001$). The responses of 41.5% of the cognitively impaired subjects (OBS 3+) to the non-test survey items were corrected by informants, compared with 10.4% of the non-impaired subjects ($\chi^2 = 33.4$; $P < 0.001$).

TABLE VI

Dependency score according to psychiatric classification (OBS, D, GA, Ph, no disorder) of subject

		Dependency score *Mean*	*s.d.*	*Skewness*
Cognitive impairment (OBS)	0–2	3.5	±6.2	2.11
	3–5	13.2	±10.9	0.42
	6+	19.0	±12.2	−0.04
Depression (D)	0–7	3.3	±6.4	2.40
	8–12	7.8	±7.9	0.82
	13+	10.1	±10.0	0.90
Generalised anxiety (GA)	0–4	3.9	±6.8	2.09
	5+	7.4	±7.5	1.17
Phobic disorder (Ph):				
Agoraphobia	—	3.7	±6.9	2.18
	+	6.6	±7.3	1.04
Social phobia	—	4.0	±7.0	2.07
	+	5.1	±6.3	1.14
Specific phobia	—	4.0	±7.0	2.06
	+	3.9	±6.4	1.66
No psychiatric disorder		2.8	±5.7	2.51

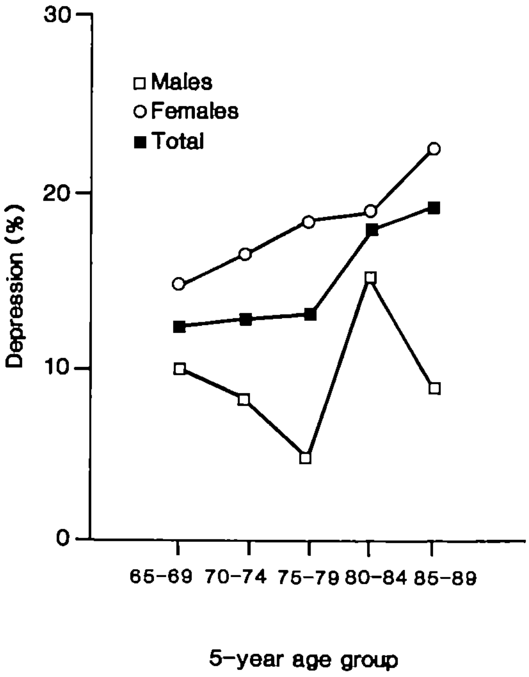

FIG. 2 Prevalence of depression (D 8+) for five-year age groups for males, females and the total sample.

TABLE VII

One-month prevalence rates (%) of depression (D) and anxiety disorders (GA, PD, Ph), according to sex and age of subject[1]

	Men			*Women*			*Total*
	65–74	*75+*	*Total men*	*65–74*	*75+*	*Total women*	
Depression (D 8+): %	8.8 (±3.5)	7.5 (±5.0)	8.4 (±2.9)	15.4 (±4.1)	18.7 (±4.9)	16.9 (±4.9)	13.5 (±2.2)
(D 13+): %	3.2 (±2.2)	1.9 (±2.6)	2.8 (±1.7)	5.1 (±2.5)	5.4 (±2.9)	5.3 (±1.9)	4.3 (±1.3)
Generalised anxiety (GA 5+): %	2.8 (±2.0)	1.9 (±2.6)	2.5 (±1.6)	4.4 (±2.3)	4.6 (±2.6)	4.5 (±1.8)	3.7 (±1.2)
Panic disorder (PD+): %	0.0 (±0.0)	0.0 (±0.0)	0.0 (±0.0)	0.0 (±0.0)	0.0 (±0.0)	0.0 (±0.0)	0.0 (±0.0)
Phobic disorder (Ph+):							
Agoraphobia: %	3.6 (±2.3)	2.8 (±3.2)	3.4 (±1.9)	11.0 (±3.6)	10.4 (±3.8)	10.7 (±2.6)	7.8 (±1.8)
Social phobia: %	0.8 (±1.1)	0.9 (±1.8)	0.8 (±0.9)	1.7 (±1.5)	1.7 (±1.6)	1.7 (±1.1)	1.3 (±0.8)
Specific phobia: %	0.8 (±1.1)	0.0 (±0.0)	0.6 (±0.8)	3.4 (±2.1)	2.5 (±2.0)	3.0 (±1.4)	2.1 (±0.9)
Total: %	4.4 (±2.5)	3.7 (±3.6)	4.2 (±2.1)	15.1 (±4.1)	12.4 (±4.2)	13.9 (±2.9)	10.0 (±2.0)
Total (D<8): %	2.4 (±1.9)	2.8 (±3.2)	2.5 (±1.6)	10.3 (±3.5)	6.2 (±3.1)	8.4 (±2.4)	6.1 (±1.6)

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[1] Figures in parentheses give 95% confidence intervals.

Depression

The prevalence rates of depression (8+ and 13+ on the D scale), classified according to sex and age of subject, are given in Table VII. Depression was significantly commoner in women at the 8+ level of severity ($\chi^2 = 12.47$; $P<0.001$), but at the 13+ level this difference in rates for men and women was not significant ($P>0.05$). Figure 2 shows the relationships between depression (D 8+) and age (5-year age groups 65–69 to 85–89) for men, women and both sexes combined. Rates rose with age in women, but in men they fell until the 75–79 age group was reached, before rising in older groups. These age-related trends were not significant at the 0.05 level. There was no significant association between depression and social class at either the 8+ or 13+ level of severity (Table V).

There was a slight but statistically significant correlation between the depression and OBS scores in this sample ($r=0.13$; one-tailed $P<0.001$); there was no significant association between cases of depression (D 8+) and cognitive impairment (OBS 3+).

Subjects with a D score of 8+ had significantly higher dependency scores than those with a D score of 0–7 ($z=8.72$; two-tailed $P<0.0001$) (Table VI). There was a significant correlation between the D and dependency scores ($r=0.37$; one-tailed $P<0.001$).

Anxiety

The prevalence rates of generalised anxiety disorder classified according to sex and age of subject are given in Table VII. The highest rate of generalised anxiety (GA 5+) was found in the female 75+ year age group, but the differences between the rates for men and women and the different age groups were not significant at the 0.05 level. There was no significant association between generalised anxiety and social class (Table V).

Generalised anxiety and depression scores were significantly associated ($r=0.68$; one-tailed $P<0.001$), as were cases of generalised anxiety (GA 5+) and depression (D 8+) ($\chi^2=149.1$; $P<0.001$). Only three subjects (9.1% of those with generalised anxiety) had depression scores of less than 8. There was no association between cognitive impairment (OBS) and generalised anxiety (GA) scores ($r=0.05$; NS). Subjects with a GA score of 5+ had higher dependency scores than those with a GA score of 0–4, but this difference was not significant at the 0.05 level ($z=1.84$; $P=0.07$).

Panic attacks were not common in this sample. Nobody met the DSM-III criteria for panic disorder (Table VII), and only one subject (0.1%) had experienced a panic attack in the month prior to interview.

The prevalence rates of agoraphobia, social phobia and specific phobia are given in Table VII. Social phobia was the least common class of phobia in this sample, and 6/12 (50%) were also agoraphobic. Agoraphobia was significantly commoner than specific phobias in the survey sample ($\chi^2=34.0$; $P<0.001$). Phobic disorders (all types) were significantly commoner in women ($\chi^2=21.21$; $P<0.001$). The rate was higher in the 65–74 year age group than in those aged 75 and over, but this difference was not significant at the 0.05 level. Phobic disorders were not significantly associated with social class (Table V).

TABLE VIII

One-month prevalence rates of particular fears in subjects with agoraphobia and specific phobias

	n	%
Agoraphobia		
Going out of the house	37	53.6
Travelling	32	46.4
Enclosed spaces	25	36.2
Being alone at home	23	33.3
Being with other people	8	11.6
Meeing other people	7	10.1
Other	11	15.9
Total	69	100.0
Specific phobia		
Spiders/insects	6	33.3
Cats/dogs	5	27.7
Blood/injury	1	5.6
Heights	1	5.6
Other	5	27.7
Total	18	100.0

Table VIII gives the prevalences of particular fears in the phobic subjects. An additional 83 subjects in the sample (9.3%) had similar fears associated with non-restricting secondary avoidance. Depression (D 8+) was significantly commoner in subjects with phobic disorders; 39.3% of phobic subjects were depressed compared with 10.6% of non-phobic subjects ($\chi^2=54.18$; $P<0.001$); 6.1% of the total sample were phobic but not depressed (Table VII). There was no association between cases of cognitive impairment (OBS 3+) and phobic disorder (Ph+) ($\chi^2=0.05$; NS).

Subjects with agoraphobia had significantly higher dependency scores ($z=4.97$; two-tailed $P<0.0001$) than those without, but there was no significant difference between the dependency scores of those with social phobias ($z=1.27$; NS) or specific phobias ($z=0.11$; NS) and the rest of the sample (Table VI). Of those subjects who were permanently housebound, 3/29 (10.3%) had agoraphobia.

Overall, 77% of the survey sample were psychiatrically fit to the extent that they did not meet the survey criteria for cognitive impairment, depression or anxiety disorders. This group of subjects had the lowest mean dependency score (Table VI), and their dependency scores were significantly different from those of subjects with cognitive impairment (OBS 3+; $z=8.6$; $P<0.0001$), depression (D 8+; $z=9.5$; $P<0.0001$) and agoraphobia ($z=6.0$; $P<0.0001$). The dependency scores of subjects with social and specific phobias did not differ significantly from those of the psychiatrically fit.

Discussion

The prevalence rates reported here are only estimates of the actual rates in the particular elderly population surveyed. Errors due to biased sampling, sample size, non-response, refusals and false-positive or false-negative case identifications are unavoidable in any survey, and in this study they have been acknowledged and quantified where possible. Sample frame bias is a potentially important source of error which may be false positive if ineligible subjects are included in the frame, or false negative if eligible subjects are excluded. The Electoral Register was chosen as the sample frame for this survey, since the local registration practices suggested that using the electoral rolls of Lewisham and North Southwark was likely to result in less overall frame bias than available alternatives such as the District Family Practitioner Committee list. Cognitive impairment did not appear to be associated with a high rate of non-inclusion in the Electoral Registers of the district, since an independent check showed that only 6% of the demented individuals presenting to one of the district psychogeriatric services during the survey period were not registered. Non-response and refusal rates were also acceptably low, and the demographic characteristics of the final sample were similar to those of the total elderly population of the district, as given by the 1981 Census. The effect of sample size upon the reliability of the reported prevalence rates of disorders for the various age groups is reflected in the 95% confidence intervals quoted in Table VII.

Comparison between surveys is difficult because methods and instruments differ between studies. To facilitate comparison, this survey chose instruments (the OBS and D scales of the CARE schedule) that had been developed, used and validated in the Cross-National Geriatric Community Survey of Gurland *et al* (1983), and that have been used and validated in other community and residential surveys of the elderly. Some of the items were slightly reworded in this survey, so the validity and reliability of these scales were checked, along with the new GA and Ph scales for identifying generalised anxiety and phobic disorders. The scales performed well against the validating criterion of a blind psychiatric diagnosis, supported in the case of the D, GA and Ph scales by a CATEGO-derived ID of 4 or more. The inter-rater reliability was high for all four scales.

If epidemiological surveys are to be useful to health care planners, they must establish explicit relationships between the prevalence of operationally defined psychiatric disorders and the resulting levels of functional impairment and dependency that determine the need for services. This study has found that the subjects meeting its criteria for cognitive impairment, depression and agoraphobia have significantly higher mean levels of dependency, which suggests that these case definitions are of both practical and theoretical value. The index of dependency used in this study is based largely on self-report, so the level associated with cognitive impairment is probably an underestimate.

Cognitive impairment

Until recently, surveys of elderly people have been reasonably consistent in finding a prevalence rate of about 5% for moderate/severe cognitive impairment in those aged 65 and over, and about 20% in those over 80. For example, in their much-quoted 1960 Newcastle survey, Kay *et al* (1964) found that 5.6% of over-65s and 22.0% of over-80s had a 'severe' organic brain syndrome. These influential figures have provided the basis for health service planning for the elderly mentally infirm for many years, but recent studies suggest that they may be too high (Ineichen, 1987). For example, Gurland *et al* (1983) found a point prevalence of 2.3% for 'pervasive dementia' in their London sample of subjects aged over 65, and Morgan *et al* (1987) reported a prevalence of 3.2% for cognitive impairment in their community sample of over-65s in Nottingham. Clarke *et al* (1986) found a prevalence of 'marked cognitive impairment' of only 4.5% in their survey of all over-75s in Melton Mowbray, Leicestershire. The prevalence rates reported here support these recent studies; 4.6% of the total sample had a CARE OBS score of 3 or more and only 1.1% scored 6 or more.

In some surveys, the lower prevalence rates quoted for 'dementia' reflect more stringent criteria for case definition. However, brief mental state tests such as the OBS scale used in this study merely detect cognitive impairment and will overestimate the prevalence of dementia, since in a proportion of cases this cognitive impairment will be the result of non-progressive or reversible conditions such as mental handicap, head injury, delirium or affective disorder. In this survey, for example, there was good evidence in at least two cases (4.9% of those with OBS 3+) that the cognitive impairment was not due to dementia; one patient was severely depressed and the other had a non-progressive deficit as the result of surgery to remove a cerebral tumour many years previously.

Another explanation for the low prevalence rates of cognitive impairment in this survey is that the sample frame excluded institutional populations, where the rates of dementia are known to be much higher. While it is true that dementia is common in those in residential and long-stay hospital care (Mann *et al*, 1984), the absolute numbers are relatively small compared with the general population; Kay & Bergmann (1980) have estimated that approximately

20% of all those with dementia live in hospitals or other institutions. However, where local services are particularly proficient at identifying elderly people with dementia and removing them into institutions, the effect on the prevalence rates of cognitive impairment in the elderly in the community will be greater. In general, excluding institutional populations from the investigation will have the greatest effect on the rates found for the very elderly, who are over-represented in institutions, but in this context Clarke *et al* (1986) found their low prevalence of cognitive impairment in a total-population sample of over-75s, both at home and in institutions.

The downward shift in the consensus estimate for the prevalence of dementia in recent years despite increased survival (Christie, 1985) may reflect a real change in incidence, although in the absence of strictly comparable methodologies we must be cautious about over-interpreting these "straws in the wind" (Arie, 1988). Incidence studies are few, and results from the total-population Lundby Study, suggesting that the incidence of dementia has fallen over the last 25 years (Hagnell *et al*, 1983), have since been called into question (Rorsman *et al*, 1986). If the incidence of dementia is falling, this may be a cohort effect, the result of new generations with different habits and experiences moving into the at-risk age groups. Factors associated with lifestyle such as diet, smoking, alcohol consumption, employment history and leisure pursuits (for example, boxing) may be relevant, particularly in the aetiology of cerebrovascular and traumatic dementias (Arie, 1988). Such factors might also account for the social class gradient in the prevalence of cognitive impairment apparent in this and other studies (Cooper & Sousa, 1983; Weissman *et al*, 1985), but the validity of survey instruments used to detect cognitive impairment also varies across educational groups, and this biases case finding to an unknown extent (Gurland, 1981).

If lifestyle factors are important in the aetiology of cognitive impairment, it might be expected that in the elderly there would be a difference in prevalence rates for men and women, since the first modern generation of women with sizeable numbers of habitual smokers, drinkers and employees is only now entering old age. On this point, the existing evidence is rather inconsistent; Neugebauer's review (1980) found that the female:male ratio in ten studies ranged from 1.64 to 0.17. It may be that age at onset of dementia is an important intervening variable; Kay & Bergmann (1980) have suggested that men are more prone to an early-onset cerebrovascular dementia, whereas women suffer mainly from later-onset 'senile dementia'. In a review of four studies they point out that 27% of the demented males were 65–74 years old, 88% of whom had been assigned a diagnosis of 'arteriosclerotic dementia'. Of the demented women, however, only 11% were 65–74 years old, with 43% of these diagnosed as 'arteriosclerotic'. This study found a significant difference in overall OBS scores for men and women, but not in the rates of cases of cognitive impairment. Of those with an OBS score of 3 or more, 28.6% of the men were in the 65–74 year age group compared with 18.5% of the women, which is consistent with the pattern described by Kay & Bergmann (1980). No attempt was made to distinguish between Alzheimer's disease and cerebrovascular dementia in the design and analysis of this survey, since a reliable distinction is not yet possible in field studies (Henderson & Jorm, 1987).

The different prevalence estimates for cognitive impairment in different studies may reflect real differences in the prevalence of dementia at different geographical sites. Very few physical or mental disorders have a uniform prevalence worldwide, and there is no reason to assume that the rates of dementia are the same everywhere. Indeed, there is evidence that the prevalence rates of dementia do in fact differ for different populations; Copeland *et al* (1987*c*) found a difference in the rates of 'pervasive dementia' for New York (4.9%) and London (2.3%) by comparable methods. By the same token, there appear to be differences between populations in the prevalence of particular types of dementia (Hasagawa *et al*, 1986). Differences in the prevalence of dementia between survey sites may reflect different survival rates, or they may be due to different rates of incidence. Future comparative studies will be important in formulating and testing aetiological hypotheses.

While estimates of the prevalence of cognitive impairment may vary between studies, there is good agreement on the rate at which it increases with age. Dementia increases exponentially rather than linearly with age (Fries, 1984), and the rates of increase at all levels of cognitive impairment in this survey (Fig. 1) agree closely with the meta-analysis of Jorm *et al* (1987), whose best-fit exponential model derived from 22 studies had a doubling time of 5.1 years, irrespective of methodology. Our findings support their suggestion that a relatively small survey of one five-year age group of septuagenarians in any given elderly population may be sufficient to estimate by projection the prevalence rates of dementia at other ages.

Depression

The overall prevalence rates of depression found in this survey are in line with those found in other comparable studies. For example, using the OARS depression scale, Blazer & Williams (1980) found 'substantial depressive symptoms' in 14.7% and 'major depressive disorder' (DSM–III) in 3.7% of their community sample of over-65s in Durham, North Carolina. Similarly, in the Cross-National survey (Gurland *et al*, 1983) the prevalence of 'pervasive depression' was 12.4% in London and 13% in New York. Applying the AGECAT diagnostic computer program to the merged London/New York data, the prevalence of 'diagnostic syndrome cases' of depressive neurosis in these subjects was 15.2%, and that of depressive psychosis was 2.5% (Copeland *et al*, 1987*b*).

As with most studies, our survey has found higher rates of depression in females, but this difference in rates for men and women was significant only for the broad category (D 8+). The absence of a significant difference in rates for men and women at the more severe level of depression (D 13+) may simply reflect the smaller number of cases, or it may indicate real differences in aetiology or mortality between mild and severe forms of the disorder.

In this survey the prevalence of depression (D 8+) in females rose across successive five-year age groups until the 85–89 age group was reached. The cross-sectional trend in males was more variable, with a drop in rates until the 75–79 age group was reached, and higher rates in subsequent five-year age groups. Overall, the rate of depression increased with age until the 85–89 age group was reached (Fig. 2), with some evidence of a decreased rate in nonagenarians. Gurland *et al* (1983) found a similar association between age and depression in males, but in their London sample the rate of depression in females fell with advancing age. Since these studies are broadly comparable, the similarities and differences are worth examining. There is agreement that the prevalence of depression troughs in the eighth decade in men. Gurland *et al* (1983) found that this age pattern was also shown by physical illness in men, and they considered that the variation of depression with age was best explained by its relationship with physical illness. It may be that the trough in the rate of depression in males is due to the increased mortality of depressed men in their sixties and early seventies, reducing the surviving population at risk of depression. Increasing chronic physical ill-health in the 70s and 80s is likely to be associated with higher rates of depression, but as the most physically and psychiatrically robust individuals survive into extreme old age depression may become less prevalent. The main difference between the studies is in the association between age and depression in females. Gurland *et al* (1983) found that their age profile was more consistent with environmental disadvantage and isolation than with physical illness, so the different findings in this study may reflect local variations in these factors. Alternatively, the differences may be due to cohort effects, since our sample of over-65s is 14 years younger than that studied by Gurland *et al* (1983). Recent cross-sectional studies in the United States have also found increased rates with age in the elderly population (Kramer *et al*, 1985).

The relationship between depression and socio-economic status in the elderly is also complex and the evidence is not consistent. Some studies, for example Warheit *et al* (1973), Blazer & Williams (1980) and Murrell *et al* (1983), have demonstrated a significant association between late-life depression and indicators of lower socio-economic status, but others have not (Gurland *et al*, 1983). The present survey found no association between occupational class and depression, either at the 8+ or the 13+ level of severity. Weissman & Myers (1978) have commented that the association between depression and social class varies according to the type of disorder surveyed; studies where symptom scales or measures of general psychiatric morbidity were used have found a consistent relationship with lower social class, but with narrower case definitions of depression this association is weak or non-existent. There were only three subjects in classes I and II in this sample, so this sample was not representative of the entire social spectrum. It may be that physical ill-health is an important intervening variable in the relationship between depression and social class in old age (Murphy, 1986).

Depression and cognitive impairment are associated in clinical populations (Post, 1962), but less is known about their relationship in community samples. This survey supports the finding of Kay *et al* (1985) that, while there may be a significant correlation at the level of symptom scores, there is no association between cases. In clinical populations, the coexistence of symptoms of depression and cognitive impairment is usually the result of depressed mood superimposed upon moderate levels of dementia, rather than impaired cognitive testing due to severe depression (Reiffler *et al*, 1982), and the same is probably true of community samples.

Anxiety

The hierarchical nature of modern classifications of anxiety states such as ICD–9 and DSM–III means that most cases of generalised anxiety disorder (GAD) are subsumed under either depression, phobic anxiety, panic, or post-traumatic stress disorders, and it no longer has much status as an independent diagnostic entity. There have been few modern estimates of its prevalence, particularly in the elderly, and differences in case definition have resulted in a wide range of values. Using a self-rated symptom checklist (the SCL-90), Uhlenhuth *et al* (1983) identified DSM-III-like 'generalised anxiety' in 7.1% of subjects aged 65-79 in the United States. In their community sample of elderly subjects living in Liverpool, however, Copeland *et al* (1987*a*), who used the GMS-AGECAT package, found a prevalence of non-phobic 'anxiety' of only 1.1%. Generalised anxiety as defined in the Guy's/Age Concern survey was present in 3.7% of the sample. The generalised anxiety score was strongly correlated with the depression score, and there was a significant association between cases at the GA 5+ and D 8+ levels. However, a small number of cases of generalised anxiety were not depressed. Tyrer (1984) has criticised the "wholesale slaughter of anxiety neurosis as a diagnostic entity", pointing out that generalised anxiety as a syndrome seems to be currently unpopular because there are no specific treatments. Under the new criteria set out in DSM-III-R (American Psychiatric Association, 1987) GAD may be diagnosed in the presence of other mood and anxiety disorders, but it remains a diagnosis of exclusion in ICD-10.

Panic disorder is a diagnostic classification that is applied to those cases of anxiety neurosis that are characterised by sudden, recurrent attacks of anxiety. Panic attacks are episodes of intense anxiety accompanied by autonomic symptoms, and often result in avoidance behaviour. For a subject to meet the DSM-III (American Psychiatric Association, 1980) criteria for panic disorder there must be three such attacks within a three-week period. As with DSM-III generalised anxiety disorder, the diagnosis can only be made in the absence of other physical or mental disorders such as depression, schizophrenia or agoraphobia. According to the ECA study, the onset of panic attacks and panic disorder peaks at 15-19 years, and they are rarely encountered in community populations of elderly people (Von Korff *et al*, 1985), a finding confirmed by this survey. Only one subject had experienced a panic attack in the month prior to interview, and he was also depressed.

With regard to phobic disorders, however, this survey supports the conclusion of Myers *et al* (1984) that they are relatively common in the elderly, particularly in women. At the Baltimore site of the ECA study, the prevalence of DSM-III phobias was 12.1% in subjects aged 65-74 and 10.1% in over-75s (Kramer *et al*, 1985). After adjustment for different diagnostic criteria, the rates reported here for phobias in non-depressed subjects are lower than these, but rather higher than those of some previous studies. Weissman *et al* (1985) found a prevalence of 3.9% for DSM-III phobic disorder (all types) in their elderly New Haven sample, Uhlenhuth *et al* (1984) found phobias broadly meeting DSM-III criteria in 3.1% of the subjects aged 65-79 in their United States sample, and the prevalence of DSM-III phobia in an elderly sample in Edmonton, Canada, was 3.0% (Bland *et al*, 1988). Others have reported even smaller prevalences of phobic anxiety in samples of elderly subjects; for example, Copeland *et al* (1987*b*), who used the GMS-AGECAT package, found a case prevalence of only 0.7%. These differences may reflect different severity criteria, since the prevalence of 5.6% reported by Copeland *et al* (1987*b*) for cases plus subcases is more comparable with this study. They may also be the result of other differences in case definition; for example, the GMS specifically asks the raters to exclude those fears that they consider reasonable in the elderly, such as fear of going out because of a fear of mugging.

For similar reasons, it is likely that health services fail to recognise phobic disorders in the elderly. Disabling fears in old people may be dismissed by the subject, their family and others as being 'reasonable for their age', and the secondary avoidance compensated for by the provision of well-meaning but misguided home support. As Bergmann (1971) has pointed out, an increased need for social support is an important expression of neurosis in old age and is often an inappropriate and ineffective response to the problem. Phobic avoidance may be a significant cause of houseboundness in the elderly; Exton-Smith *et al* (1976) found that 20% of his sample of housebound elderly had no physical reason to keep them indoors, 'nervousness' and 'loss of confidence' being given as explanations instead. In this sample, agoraphobia was associated with significantly higher dependency scores, and 10.3% of those who were permanently housebound were agoraphobic. Specific phobias were not associated with high levels of functional impairment.

Elderly people are properly cautious of threats and danger in their environment, but there is no evidence to suggest that a chronic state of fear with disabling generalised avoidance is a normal or inevitable consequence of the ageing process. Although some fears, for example, fear of street crime (Harris, 1975), are common in the elderly, the rates of phobic disorder found in this study are low in comparison. Less than 20% of the total sample coped with frightening objects or situations by avoiding them.

Over one-third of subjects with phobic disorders in this sample were also depressed, which emphasises their clinical significance since in many cases this depression appeared to be secondary to the restrictions imposed by their phobic avoidance. Little is known about the particular causes and effects of phobic disorders in old age, and the phobic subjects identified in this sample are being studied further.

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Appendix I

(A) Generalised anxiety — Score

(1) (a) Have you had any headaches in the past month?
IF YES: Do you know what brought it/them on?
Did worrying help to bring it/them on?
(b) Has worry brought on any other aches or pains in the past month?
Headache/other pains due to worry — 1

(2) In the past month have you felt so fidgety or restless that you couldn't sit still?
IF YES: Do you know what brought it on?
Was it due to worry, fear or something else?
Restlessness due to worry/fear/anxiety — 1

(3) Could you tell me if you've had any of the following symptoms in the past month?
(a) Noticed your heart racing or thumping
(b) A sinking feeling in your stomach
(c) Difficulty catching your breath, even though you weren't exerting yourself
(d) A choking lump in your throat
(e) Felt as if you were going to faint
(f) Attacks of hot or cold feelings, or sweating or blushing
(g) Any tingling or numbness of the fingers or toes.
IF YES: Do you know what brought it on?
Was it due to worry, fear or something else?
One or more symptoms due to worry/fear/anxiety — 1

(4) How often, if at all, have you worried in the past month?
Never — 0
Some days — 0
Most days — 1
All the time — 1

(5) In the past month, have you had any difficulty getting up in the morning because you felt afraid to face the day?
Has felt afraid to face the day — 1

(6) In general, would you describe yourself as a worrier?
Admits to being a worrier — 1

(7) Have you felt on edge, strung up or mentally tense in the past month?
Never — 0
Some days — 0
Most days — 1
All the time — 1

(8) Do you take anything to help you relax? What about sedative tablets or alcohol?
Takes medication or alcohol to relax — 1

(9) Have you had any difficulties with sleeping lately, that is, in the past month?
IF YES: What is it that prevents you from sleeping, or wakes you up?
Sleep difficulty due to worry/anxious thoughts — 1

What goes through your mind when you are lying awake? Do you have trouble sleeping because you feel tense, or have worrying thoughts?

(10) Have you in the past month had any frightening dreams that have woken you up
Has had nightmare in past month — 1

(11) During the past month, have you felt more irritable or angry than usual, or about the same as usual, or less angry or irritable?
More angry/irritable — 1

(B) Phobic disorders

(1) Some people get very worried or frightened by particular situations. I'm going to read out a number of things and I'd like you to tell me, please, for each one whether that kind of thing usually makes you feel *very* worried or anxious, or not.
(a) Going out of the house/flat
(b) Being alone at home
(c) Enclosed spaces, places that are shut in
(d) Being with other people
(e) Having to meet other people
(f) Any kind of travelling
(g) Is there any other situation that makes you feel very worried or anxious?

IF YES TO ANY OF THE ABOVE:
Have you actually (been in feared situation/s) in the past month?

IF YES: What kind of feeling did you get when you were?
For example, did your heart thump, did you go hot and cold, or what?

IF NO: Have you avoided (the feared situation/s) in the past month, or would you have avoided it if the situation had arisen? Does the fact that you have to avoid (the feared situation/s) mean that you can't do certain things that you'd like to do, or need to do?

(2) Do you have any special fears, like some people are afraid of spiders, birds or blood?

IF YES:
Have you actually been frightened by (feared object/s) in the past month?

IF YES: What kind of feeling did you get when it happened?
For example, did your heart thump, did you get a choking feeling in your throat, or what?

IF NO: Have you avoided (feared object/s) in the last month, or would you have avoided it/them if you'd been in a situation where you could have seen one?
Does the fact that you avoid (feared object/s) mean that you can't do certain things that you'd like to do, or need to do?

(C) Panic attacks
Some people occasionally get feelings of anxiety or dread that are so strong that they simply have to do something to stop them, like running away. Have you felt like that in the past month?

IF YES: What did that anxiety or dread feel like?
For example did you get a thumping of the heart, or what?
How many of these attacks have you had in the past month?

Appendix 2

Dependency Score
This is derived from the 13 items listed below, each scored as follows:

(a) On your own without difficulty	0
(b) On your own with difficulty	1
(c) Only with help	2
(d) not at all	3

(1) Can you go out of doors?
(2) Can you use public transport?
(3) Can you go shopping for food or clothes?
(4) Can you cook a main meal?
(5) Can you wash clothes?
(6) Can you clean windows inside?
(7) Can you deal with any medicines or tablets that you might have to take?
(8) Can you handle your own money or finances?
(9) Can you feed yourself?
(10) Can you dress and undress yourself?
(11) Can you get in and out of bed?
(12) Can you have a bath or shower?
(13) Can you get around the house/flat?

References

American Psychiatric Association (1980) *Diagnostic and Statistical Manual of Mental Disorders (3rd edn)*. Washington: APA.

—— (1987) *Diagnostic and Statistical Manual of Mental Disorders (3rd edn, revised)*. Washington: APA.

Arie, T. (1988) Questions in the psychiatry of old age. In *Research and the Ageing Population*, (eds D. Evered & J. Whelan), Ciba Foundation Symposium 134. Chichester: John Wiley.

Bergmann, K. (1971) The neuroses of old age. In *Recent Developments in Psychogeriatrics*, (eds D. W. K. Kay & A. Walk) Kent: Headley Bros.

Blazer, D. & Williams, C. D. (1980) Epidemiology of dysphoria and depression in an elderly population. *American Journal of Psychiatry*, **137**, 439–444.

Bland, R. C., Newman, S. C. & Orn, H. (1988) Prevalence of psychiatric disorders in the elderly in Edmonton. *Acta Psychiatrica Scandanavica* (Supplement 338), 57–63.

Cartwright, A. & Smith, C. (1987) Identifying a sample of elderly people by a postal screen. *Age and Ageing*, **16**, 119–122.

Catalan, J., Gath, D. H., Bond, A., *et al* (1988) General practice patients on long-term psychotropic drugs: a controlled investigation. *British Journal of Psychiatry*, **152**, 399–405.

Christie, A. B. (1985) Survival in dementia: a review. In *Recent Advances in Psychogeriatrics* (ed. T. Arie). London: Churchill Livingstone.

Clarke, M., Lowry, R. & Clarke, S. (1986) Cognitive impairment in the elderly: a community survey. *Age and Ageing*, **15**, 278–284.

Cooper, B. & Sousa, N. (1983) Psychische Erkrankung in der Altenvolkerung: Eine Epidemiologische feldstudie in Mannheim. *Nervenarzt*, **54**, 239–249.

Copeland, J. R. M., Kelleher, M. J., Kellett, J. M., *et al* (1976) A semi-structured clinical interview for the assessment of diagnosis and mental state in the elderly: The Geriatric Mental State Schedule. I: Development and reliability. *Psychological Medicine*, **6**, 439–449.

——, Dewey, M. E., Wood, N., *et al* (1987*a*) Range of mental illness among the elderly in the community: prevalence in Liverpool using the GMS-AGECAT package. *British Journal of Psychiatry*, **150**, 815–823.

——, Gurland, B. J., Dewey, M. E., *et al* (1987*b*) The distribution of dementia, depression and neurosis in elderly men and women in an urban community: assessed using the GMS-AGECAT package. *International Journal of Geriatric Psychiatry*, **2**, 177–184.

——, ——, ——, *et al* (1987*c*) Is there more dementia, depression and neurosis in New York? A comparative study of the elderly in New York and London using the computer diagnosis AGECAT. *British Journal of Psychiatry*, **151**, 466–473.

Exton-Smith, A. N., Stanton, B. R. & Windsor, A. C. M. (1976) *Nutrition of Housebound Old People*. London: King Edward's Hospital Fund.

Fries, J. F. (1984) The compression of mortality, Benjamin Gompertz, the two types of chronic disease and health policy. In *Forum Proceedings: Exploring New Frontiers of US Health Policy*. New Jersey: UMDNJ-Rutgers Medical School.

Gurland, B. J. (1981) The borderlands of dementia: the influence of sociocultural characteristic on rates of dementia occurring in the senium. In *Aging Vol 15. Clinical Aspects of Alzheimer's Disease and Senile Dementia* (eds N. E. Miller, & G. D. Cohen). New York: Raven Press.

——, Kuriansky, J. B., Sharpe, L., *et al* (1977) The Comprehensive Assessment and Referral Examination (CARE) – rationale, development and reliability. *International Journal of Aging and Human Development*, **8**, 9–42.

——, Copeland, J., Kuriansky, J., *et al* (1983) *The Mind and Mood of Aging*. London: Croom Helm.

——, Golden, R. R., Teresi, J. A., *et al* (1984) The Short-CARE: an efficient instrument for the assessment of depression, dementia and disability. *Journal of Gerontology*, **39**, 166–169.

Hagnell, O., Lanke, J., Rorsman, B., *et al* (1983) Current trends in the incidence of senile and multi-infarct dementia. *Archiv für Psychiatrie und Nervenkrankheit*, **233**, 423–438.

Harris, L. (1975) *The Myth and Reality of Aging in America* Washington: National Council on Aging.

Hasagawa, K., Homma, A. & Imai, Y. (1986) An epidemiological study of age-related dementia in the community. *International Journal of Geriatric Psychiatry*, **1**, 45–55.

Henderson, A. S. & Jorm, A. F. (1987) Is case ascertainment of Alzheimer's disease in field surveys practicable? *Psychological Medicine*, **17**, 549–555.

——, & Macfadyen, D. M. (1985) Psychogeriatrics in the programme of the World Health Organisation. In *Recent Advances in Psychogeriatrics*, (ed. T. Arie). London: Churchill Livingstone.

Hunt, A. (1978) *The Elderly at Home*. London: HMSO.

Ineichen, B. (1987) Measuring the Rising Tide. How many dementia cases will there be by 2001? *British Journal of Psychiatry*, **150**, 193–200.

Jorm, A. F., Korten, A. E. & Henderson, A. S. (1987) The prevalence of dementia: a quantitative integration of the literature. *Acta Psychiatrica Scandanavica*, **76**, 465–479.

Kay, D. W. K., Beamish, P. & Roth, M. (1964) Old age mental disorders in Newcastle upon Tyne. Part I: A study of prevalence. *British Journal of Psychiatry*, **110**, 146–158.

——, & Bergmann, K. (1980) Epidemiology of mental disorders in the aged. In *Handbook of Studies of Mental Health and Aging* (eds J. E. Birren & R. B. Sloane). Prentice Hall: Englewood Cliffs.

——, Henderson, A. S., Scott, R., *et al* (1985) Dementia and depression among the elderly living in the Hobart community: the effect of the diagnostic criteria on the prevalence rates. *Psychological Medicine*, **15**, 771–788.

Kramer, M., German, P. S., Anthony, J. C., *et al* (1985) Patterns of mental disorders among the elderly residents of Eastern Baltimore. *Journal of the American Geriatrics Society*, **33**, 236–245.

Mann, A. H., Graham, N. & Ashby, D. (1984) Psychiatric illness in residential homes for the elderly: a survey in one London Borough. *Age and Ageing*, **13**, 257–265.

Morgan, K., Dallosso, H. M., Arie, T., *et al* (1987) Mental health and psychological well-being among the old and very old living at home. *British Journal of Psychiatry*, **150**, 801–807.

Murphy, E. (1986) Social factors in late life depression. In *Affective Disorders in the Elderly*, (ed. E. Murphy). London: Churchill Livingstone.

Murrell, S. A., Himmelfarb, S. & Wright, K. (1983) Prevalence of depression and its correlates in older adults. *American Journal of Epidemiology*, **117**, 173–185.

Myers, J. K., Weissman, M. M., Tischler, G. L., *et al* (1984) Six-month prevalence of psychiatric disorders in three communities: 1980–1982. *Archives of General Psychiatry*, **41**, 959–967.

Neugebauer, R. (1980) Formulation of hypotheses about the true prevalence of functional and organic psychiatric disorders among the elderly in the US. In *Mental Illness in the United States: Epidemiological Estimates*, (eds B. P. Dohrenwend & B. S. Dohrenwend. New York: Praeger.

Office of Population Censuses and Surveys (1970) *Classification of Occupations, 1970*. London: HMSO.

Post, F. (1962) *The Significance of Affective Symptoms in Old Age*. London: Oxford University Press.

Reiffler, B. V., Larson, E. & Hawley, R. (1982) Coexistence of cognitive impairment and depression in geriatric outpatients. *American Journal of Psychiatry*, **139**, 623–626.

Rorsman, B., Hagnell, O. & Lanke, J. (1986) Prevalence and incidence of senile and multi-infarct dementia in the Lundby Study: a comparison between the time periods 1947–1957 and 1957–1972. *Neuropsychobiology*, **15**, 122–129.

Skegg, D. G., Doll, R. & Perry, J. (1977) Use of medicines in general practice. *British Medical Journal*, **i**, 1561–1563.

Statistical Package for the Social Sciences (10th edn) (1986) Chicago: SPSS Inc.

Todd, J. & Butcher, B. (1982) *Electoral Registration in 1981*. London: OPCS.

Tyrer, P. (1984) Classification of anxiety. *British Journal of Psychiatry*, **144**, 78–83.

Uhlenhuth, E. H., Balter, M. B., Mellinger, G. D., *et al* (1983) Symptom checklist syndromes in the general population. *Archives of General Psychiatry*, **40**, 1167–1173.

——, Balter, M. B., Mellinger, G. D., *et al* (1984) Anxiety disorders: prevalence and treatment. *Current Medical Research and Opinion*, *8*, Supplement 4, 37–47.

Von Korff, M. R., Eaton, W. W. & Keyl, P. M. (1985) The epidemiology of panic attacks and panic disorder. *American Journal of Epidemiology*, **122**, 970–981.

Warheit, G. J., Holzer, C. E. & Schwabb, J. J. (1973) An analysis of social class and racial differences in depressive symptomatology: a community study. *Journal of Health and Social Behaviour*, **14**, 291–299.

Weissman, M. M. & Myers, J. K. (1978) Affective disorders in a US urban community. *Archives of General Psychiatry*, **35**, 1304–1311.

——, Myers, J. K., Tischler, G. L., *et al* (1985) Psychiatric disorders (DSM-III) and cognitive impairment among the elderly in a US urban community. *Acta Psychiatrica Scandanavica*, **71**, 366–379.

Wing, J. K. (1976) A technique for studying psychiatric morbidity in in-patient and out-patient series and in general population samples. *Psychological Medicine*, **6**, 665–671.

——, Cooper, J. E. & Sartorius, N. (1974) *The Measurement and Classification of Psychiatric Symptoms*. Cambridge: Cambridge University Press.

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Depression Before and After Age 65

A Re-examination

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Systematic and detailed psychopathological examination of 400 consecutive primary major depressives failed to confirm common clinical stereotypes which ascribe greater somatisation, hypochondriasis, agitation, psychotic tendencies, and chronicity to old age. Those above 65 were more likely to suffer from single episodes of depression that were often precipitated, whereas subjects whose illness began earlier were more likely to express depression as part of a recurrent unipolar or bipolar disorder, with higher rates of affective temperamental pathology and familial affective illness. The acute clinical picture was relatively uniform in older and younger depressives and, taken together with the other findings, tends to favour a spectrum model of primary mood disorders.

Recognition and diagnosis of mood disorders in the elderly is influenced by various factors. The clinical assessment is often complicated by the fact that in the elderly mental and physical pathology often coexist (Kukull *et al*, 1986). Furthermore, certain normal mental concomitants of ageing could be erroneously labelled 'depressive'.

It is generally believed that depressions in the elderly display special characteristics: greater agitation (Winokur *et al*, 1973), 'atypical' and masked features (Goldfarb, 1967; Finlayson & Martin, 1982; Shamoian, 1985), a high number of somatic symptoms (Saltzman & Shader, 1978; Nielsen & Williams, 1980; Winokur *et al*, 1980; Katon, 1982) and hypochondriacal worries (Gurland, 1976; Goldstein, 1979; Steuer *et al*, 1980; Busse & Blazer, 1980; Pichot & Pull, 1981), a suspicious attitude and ideas of reference (Placidi *et al*, 1984), and a tendency to chronic evolution (Kukull *et al*, 1986). A methodological limitation of the studies mentioned is that most, although not all, derive from in-patient samples. It is also uncertain whether the patterns reported are typical of old-age depression or are derived from other psychopathological conditions accompanying depression in old age.

The present study was designed to test the foregoing assumptions about the psychopathology of depression in a sample of patients with primary mood disorders selected on the basis of full-blown depressive episodes at index interview and the absence of pre-existing other major psychiatric and medical-neurological disorders. We also followed Post's (1987) suggestion of comparing patients both by index age and age of onset of first depression.

Method

This study is based on a consecutive series of 405 clinically depressive patients seen at the Institute of Clinical Psychiatry at the University of Pisa, Italy, and affiliated clinical facilities over an 18-month period. We receive patients in about equal proportions from self-referrals, family practitioners, other medical specialists, and psychiatrists, as well as through former patients.

All patients had primary major depression, and they were obtained after the exclusion of those with pre-existing or concurrent dementias, mental retardation, alcoholism and other clinically significant substance-use disorders, schizophrenia, somatisation hysteria, anorexia nervosa, and depression secondary to panic, obsessive–compulsive, social phobic and agoraphobic disorders. Diagnoses were based on DSM-III-R criteria (American Psychiatric Association, 1987). We also excluded those with established neurological diagnoses (e.g. Parkinson's disease, multiple sclerosis, brain tumour), and those with serious or disabling medical conditions; however, hypertension under good medical control was not grounds for exclusion. Patients who refused or who were unable to undergo the standard evaluation were also excluded.

For the assessment of symptoms project psychiatrists completed the Hamilton Rating Scale for Depression (HRSD; Hamilton, 1967), and the Retardation Rating Scale (RRS) of Widlöcher (1983), and patients completed the Hopkins Symptoms Check-List (HSCL–90) of Derogatis *et al* (1973).

Diagnostic subtyping of subjects was accomplished with the Semistructured Interview for Depression (SID; Cassano *et al*, 1987), which represents a collaborative effort between the Institute of Clinical Psychiatry of the University of Pisa, and the Section of Affective Disorder at the University of Tennessee. It was developed to diagnose major depressive episodes (MDEs) (American Psychiatric Association, 1987) and to collect systematic anamnestic data on number and duration of previous episodes, number of suicide attempts, temperamental aspects, residual and inter-episodic phenomena, the response to previous treatments, 'stressors' related to the onset of the index episode, the presence of melancholia (or endogenous clinical features), and congruent and incongruent psychotic features; family history data are collected by Winokur's approach as incorporated into the family history method of the Research Diagnostic Criteria (Andreasen *et al*, 1977). The major innovation in this instrument is the provision of operational criteria for depressive and hyperthymic temperaments, representing the University of Tennessee modification (Akiskal & Mallya, 1987) of Schneider's (1958) descriptions. The depressive temperament requires the presence of at least five of the following items: (a) gloomy, pessimistic, humourless or incapable of fun; (b) quiet, passive and indecisive; (c) sceptical, hypercritical or complaining; (d) brooding and given to worry; (e) conscientious or self-disciplining; (f) self-critical, self-reproaching, or self-derogatory; (g) preoccupied with inadequacy, failure and negative events to the point of morbid enjoyment of one's failures. As for the hyperthymic temperament, it requires the presence of at least five of the following items: (a) irritable, cheerful, overoptimistic or exuberant; (b) naïve, overconfident, self-assured, boastful, bombastic or grandiose; (c) full of plans, improvident, rushing off with restless impulse; (d) over-talkative; (e) warm, people-seeking or extroverted; (f) overinvolved and meddlesome; (g) uninhibited, stimulus-seeking or promiscuous.

Based on exclusion of pre-existing non-affective conditions, family history, subtype of temperament, history of hypomanic or manic episodes, and recurrence of episodes, the SID decision tree identifies the following subtypes of primary depression modified from the classificatory schema of Akiskal (1983*a*, *b*): (a) classic or bipolar I (BI) disorder, with a history of full-blown manic symptomatology; (b) bipolar II (BII) disorder, defined as MDE preceded or followed by hypomania or hyperthymic temperament; (c) bipolar III (BIII) disorders, in which patients do not meet BI or BII criteria but have first-degree relatives with bipolar illness; (d) recurrent unipolar (RU) depression, in the absence of bipolar family history and with neither hypomania nor hyperthymic temperament; (e) single episode (SE) depression. Such subtyping permits purer separation of unipolar and bipolar subtypes than achieved in other diagnostic systems.

The SID instrument derived in part from other operationalised procedures with published reliabilities (Andreasen *et al*, 1977; American Psychiatric Association, 1987), as well as new procedures introduced by us to address the temperamental foundations of mood disorders and the assignment of patients into the proposed bipolar and depressive subtypes. We have now systematically used this instrument for over three years, we have conducted at least 700 interviews, and psychiatrists participating in this series of studies have extensive and systematic training in the interview, which has proven reliable (Cassano *et al*, 1987). The semi-structured face-to-face interview, which lasts 30–60 minutes, is well accepted by patients. For final diagnostic subtyping, all the clinical information obtained face-to-face interviews by two experienced psychiatrists is presented to the senior Italian psychiatrist on our team (GBC), and he, during a briefer face-to-face interview, assigns consensus diagnoses.

For statistical comparisons we used χ^2 analysis for categorical data and Student's t-test for dimensional variables. We conservatively used two-tailed statistics. When data departed from Gaussian form, we reanalysed dimensional variables with the non-parametric Mann–Whitney test.

Results and comments

According to the diagnostic classes of the SID, the original sample of depressives included 25 (6.3%) BI, 107 (26.8%) BII, 174 (43.5%) RU, and 94 (23.5%) SE. There were only five patients (1%) with BIII disorder, and for this reason this group has been excluded from further consideration in the statistical analyses.

The remaining sample included 359 out-patients and 41 in-patients (total $n=400$), reflecting the fact that depression seen today represents largely an ambulatory illness. There were 127 (31.8%) males and 273 (68.3%) females, and the mean age was 50.6 (s.d. 13.8).

Seventy patients (17.5%) were over 65 years of age (Table I). In these patients, age of onset, the duration of the illness, the number of previous depressive episodes and the number of hospital admissions were higher than in those under 65. This may be simply a reflection of the fact that the elderly have had more opportunity to have high rates in all these variables. Females predominated in both samples, comprising 66.7% of those below 65 and 75.7% of those above 65 ($\chi^2=1.78$, d.f.$=2$, NS).

TABLE I

Demographic and longitudinal features of depressed patients under and over 65 years of age[1]

	Age <65 (n=330)		*Age ≥65 (n=70)*	
	Mean	*s.d.*	*Mean*	*s.d.*
Age: years	46.6	11.6	69.5	4.1
Age at onset: years	35.7	13.1	53.0	15.1
Duration of illness: years	10.9	10.7	16.5	15.3
Age at first treatment: years	36.6	12.7	54.8	14.6
Number of depressive episodes	4.1	4.7	5.7	6.8
Number of manic episodes	0.2	1.0	0.1	0.6
Number of hospital admissions	1.1	2.6	2.1	3.7

[1] Significance tests were not undertaken because any differences would be expected from the subdivision of the sample by current age.

TABLE II
Diagnostic distribution in depressed patients according to age of patients and age at onset

	BI	*BII*	*RU*	*SE*	χ^2	*d.f.*	P
Age							
<65 ($n=330$)	7.3	27.6	42.1	23.0	4.64	(3)	NS
≥ 65 ($n=70$)	1.4	22.9	50.0	25.7			
Age at onset							
<40 ($n=217$)	9.7	30.9	47.5	12.0	67.10	(6)	<0.001
40–59 ($n=141$)	2.8	24.1	44.7	28.4			
≥ 60 ($n=42$)	0.0	14.3	19.0	66.7			

Diagnostic distribution

In patients over 65, BI disorder, with full-blown manic episodes, was less frequently observed than recurrent forms and single episodes (Table II). However, BII, defined by depressive episodes which alternate with hypomanic episodes or which arise from a previous hyperthymic temperament, was equally prevalent in both age groups.

As to age at onset of the illness, Table II shows that none of the patients with onset after 60 belonged to BI. This finding confirms reports in the literature that manic episodes are typical of early-onset mood disorders (Depue & Monroe, 1978; Angst, 1966; Akiskal *et al*, 1983; Coryell *et al*, 1985), and that geriatric mania observed by others (Roth, 1976; Shulman & Post, 1980; Glasser & Rabins, 1984) either has strong organic determinants or represents the excited pole of a recurrent depression that began earlier. In our sample, the proportion of recurrent (unipolar) depressions shows a gradual and significant decline with age, whereas single episode cases show a significant increase with age. Obviously, the class of major depression, single episode, as defined by the SID, represents a heterogeneous group of patients, in that some cases might represent the onset of recurrent mood disorders. However, the high percentage (66.7%) of single episodes with age at onset suggests that recurrent mood disorders are less likely to begin in old age for the first time.

Course, inter-episodic characteristics, and temperament

The evolution toward chronicity (duration of episode over two years) (American Psychiatric Association, 1987) does not seem to be a typical characteristic of elderly patients in our sample (Table III). Furthermore, complete inter-episodic recovery is not significantly different in the two groups. These data confirm earlier findings by Akiskal (1982), and tend to refute the conventional view of a greater tendency to

TABLE III
Chronic course, hypomania, temperament, inter-episodic characteristics, melancholia and psychotic features in depressed patients under and over 65 years of age

	Age <65 *(n = 330)* %	*Age* ≥ 65 *(n = 70)* %	χ^2	*d.f.*	P
Chronic course (>24 months)	14.8	18.6	0.36	(1)	NS
Complete remission between episodes[1]	54.8	51.0	0.11	(1)	NS
Hypomania	23.0	14.3	2.12	(1)	NS
Pharmacological hypomania	9.2	2.9	2.45	(1)	NS
Hyperthymic temperament	14.2	11.4	0.18	(1)	NS
Depressive temperament	38.8	34.3	0.32	(1)	NS
Melancholia	70.6	74.3	0.22	(1)	NS
Psychotic features					
Congruent	7.9	2.9	1.53	(1)	NS
Incongruent	1.2	1.4	0.20	(1)	NS

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[1] The numbers of patients are smaller here (<65, 239; ≥65, 49), because, by definition, this item excludes the SE category, and BII patients with only one major depressive episode.

TABLE IV

Hypomania, temperament and stressors in depressed patients according to age at onset

	Age at onset			χ^2	d.f.	P
	<40 (n=217) %	40–59 (n=141) %	≥60 (n=42) %			
Hypomania	28.6	14.9	7.1	15.20	(2)	<0.01
Pharmacological hypomania	12.0	4.3	2.4	8.88	(2)	<0.05
Hyperthymic temperament	15.2	13.5	7.1	1.94	(2)	NS
Depressive temperament	44.2	31.2	28.6	7.93	(2)	<0.05
Stressors	47.7	63.8	59.5	9.42	(2)	<0.01

chronicity of mood disorders in the elderly (Kukull *et al*, 1986); probably a greater part of the chronicity of depression in old age reported in the literature could be accounted for by mixed samples that combine secondary depressions with primary mood disorders. As reported by Ciompi (1969), uncomplicated geriatric depressions tend to have a good prognosis.

Unlike mania, which is clearly more common in younger age groups (Table II), hypomanic and hyperthymic tendencies are about equally prevalent in those above 65 and those below 65 (Table III). Nor is there a significant difference in pathological depressive temperaments between the two age groups. However, judging from the distribution of the age at onset for cases with BI and BII disorders in younger age groups (Table II), we would suggest that in patients over 65, hypomanic and hyperthymic tendencies represent cases accumulated from younger age groups. This is further supported by the data in Table IV on the differential distribution of such tendencies in depressions with different ages of onset.

Stressors

Stressors in the six months before the index episode were significantly less apparent in depressives whose illness began before age 40 than in those whose illness began after 40 (Table IV). As earlier age of onset of depression is associated with bipolar or recurrent depressive (unipolar) subtypes, precipitation by psychosocial events appears less likely in such recurrent mood disorder subtypes. The opposite can be said about the less recurrent depressions of old age (Angst, 1966; Blazer & Williams, 1980; Murphy, 1982).

We cannot comment on the contribution of somatic factors to the origin of geriatric depression (Jacoby *et al*, 1981), because to obtain a 'primary' sample of depressives we excluded those with concomitant serious physical illness.

Family history

Familial rates of alcoholism and schizophrenia were not significantly different for different ages of onset (Table V). Although familial bipolar and unipolar rates, taken individually, were not significantly different in probands with different ages at onset, total familial affective illness (which combined bipolar and unipolar familial rates) was significantly higher in those with earlier age at onset, showing a significant gradient across the three age-at-onset groups examined in Table V. These findings are in line with the existing literature (Angst, 1966; Hopkinson & Ley, 1969; Mendlewicz, 1976).

TABLE V

Family history (first degree) in depressed patients according to age at onset

	Age at onset			χ^2	d.f.	P
	<40 (n=217) %	40–59 (n=141) %	≥60 (n=42) %			
Alcoholism	8.3	7.8	4.8	0.61	(2)	NS
Schizophrenia	1.4	0	2.4	2.55	(2)	NS
Bipolar	5.5	4.3	0	2.53	(2)	NS
Unipolar	40.1	31.2	28.6	3.99	(2)	NS
Total, bipolar + unipolar	45.6	35.5	28.6	6.33	(2)	<0.05

Melancholia and psychotic features

Episodes of depression were of the melancholic type in more than two-thirds of the index episodes in both the over-65s and the under-65s (Table III). Psychotic features were observed somewhat more often, though not significantly so, in young patients, probably reflecting an association with bipolar disorder of younger age of onset (Akiskal *et al*, 1983). Thus, as in the study by Murphy (1983), geriatric depressions are not characterised by high rates of psychosis if one examines a consecutive series that includes both in-patients and out-patients, as in the present study.

Symptoms

Objective measures of depression on the HRSD were generally comparable in older and younger depressives, except that the factor 'loss of weight' attained higher values in the patients over 65 (mean = 0.6, s.d. = 0.6, v. mean = 0.4, s.d. = 0.7; $P<0.05$) whereas 'cognitive disorders' – a factor that includes such items as self-blame and suicidal ideation – was higher in patients under 65 (mean = 0.6, s.d. = 0.4, v. mean = 0.5, s.d. = 0.3; $P<0.05$). This would reinforce the generally held clinical view that weight loss is more a symptom of old-age depression (Placidi *et al*, 1984), whereas cognitive factors might reflect recurrences of depressive episodes more characteristic of younger age groups. The fact that such major HRSD factors as 'anxiety', 'diurnal variation', 'psychomotor retardation', and 'sleep disorders' did not differ significantly between the two age groups suggests some uniformity of core depressive symptomatology across ages. However, with a more detailed examination of psychomotor retardation according to RRS, we found that the elderly were somewhat more retarded: RRS showed a somewhat higher total score in patients over 65 (mean = 20.7, s.d. = 9.2, v. mean = 18.1, s.d. = 9.1; $P<0.05$), contributed largely by such items as slow gait (mean = 1.4, s.d. = 1.0, v. mean = 1.0, s.d. = 0.9; $P<0.01$), slow movements (mean = 1.3, s.d. = 0.9, v. mean = 1.0, s.d. = 0.9; $P<0.05$), and slow passage of time (mean = 1.8, s.d. = 1.3, v. mean = 1.4, s.d. = 1.3; $P<0.05$), and being less rich in verbalisation (mean = 1.4, s.d. = 1.1, v. mean = 1.1, s.d. = 1.0; $P<0.05$). These modest differences do not necessarily indicate symptomatological differences between the older and younger depressives, but may simply reflect the normal effects of ageing.

With respect to self-evaluation by means of HSCL–90, no overall significant differences are shown between the two age groups in eight of the nine factors: 'somatisation', 'obsessive–compulsive', 'interpersonal sensitivity', 'depression', 'anxiety', 'phobic anxiety', 'paranoid ideation' and 'psychoticism'. Only on the factor 'hostility–anger' was there a significant difference, the score being higher in younger patients (mean = 0.9, s.d. = 0.8, v. mean = 0.7, s.d. = 0.5; $P<0.01$), suggesting a possible association with bipolarity.

As some of the psychometric data departed somewhat from Gaussian form, we re-tested them with the non-parametric Mann–Whitney test. The results were identical in all instances except for greater fatigability in the older depressives measured on the RRS ($P<0.05$).

No further differences in symptomatology were revealed when the patients with first onset after 65 ($n=20$) were compared with patients over 65 whose depression had begun earlier ($n=50$).

Conclusions

In the present study, which focused on a consecutive and very large series of patients with rigorously defined primary major depression, neither chronicity, nor inter-episodic residuals, were related to old age. It is possible that the clinical picture of greater chronicity of depression in old age is derived from in-patient or clinical samples in which depressions have been mixed with other psychiatric and physical disorders.

It is also noteworthy that the psychomotor differences are in the opposite direction from predictions in the literature, and that agitation, and paranoid and obsessive–compulsive symptoms, long thought to be typical of elderly depressives (Saltzman & Shader, 1978; Goldstein, 1979; Steuer *et al*, 1980) do not emerge as hallmarks of depressed patients over 65 years in the present sample. Thus, we could not confirm prevalent clinical stereotypes. Melancholic and psychotic features did not distinguish the elderly depressives from their younger contemporaries; if anything, younger depressives tended to have greater mood-incongruence. Furthermore, our elderly depressives, rather than being agitated, displayed greater motor retardation. It would appear that the 'classic' clinical description of agitated depression in old age is based on more severe in-patient depressive samples, or the inclusion of out-patients with mixed anxiety and depressive disorders.

Few relatively minor differences in symptoms emerged between geriatric depressives and their younger counterparts: these involved greater hostility, self-blame and suicidal ideation in the younger patients, and greater weight loss in the elderly. The weight loss in the elderly may reflect not so much pathoplastic effects of ageing but the fact that more of the elderly were unipolar.

It could be argued that the lack of differences between younger and older depressives in the present study represents an artefact of selection that excluded those with concomitant somatic pathology and those with extensive pre-morbid psychopathology. Such patients could conceivably differ, in important ways, from younger patients without such pathologies. However, we excluded such patients precisely because we were interested in the clinical phenomenologies of mood disorders at different ages uncontaminated by concurrent non-affective disorders. The fact that our sample was predominantly outpatient also probably contributed to the lack of major differences between younger and older depressives. We feel, however, that such an ambulatory focus is justified, as it represents current clinical reality. The possible bias introduced by studying a clinical sample referred to a major university medical centre is generic to all clinical research undertaken at such centres; certainly an epidemiological sample would have been, in some respects, preferable. We, therefore, submit that the results reported by us are most relevant to patients who come to the clinical attention of psychiatrists through a variety of referral mechanisms. Such a focus on a clinical population can supplement insights into age and depression gained through the use of epidemiological samples.

The major differences emerging from this study concern diagnostic subtypes of primary mood disorder and their familial distribution at different ages at onset. Thus, bipolar I and bipolar II disorders and recurrent (unipolar) depression typically arise before age 65 and show high familial prevalence of mood disorders; this is particularly true for the bipolar I subtype characterised by mania. Single-episode depression, by contrast, was significantly more common after age 65; environmental factors, such as stressors identified within six months of the onset of depression, were more common in this subtype. These data tend to support a spectrum model of primary mood disorders, where differences in genetic risk favour earlier in life the appearance of disorders which are less precipitated by external factors and have frequent episodes, especially bipolar disorders – with heavy constitutional load manifesting in temperamental pathology – and later in life the appearance of single-episode varieties, which are genetically less penetrant and are environmentally precipitated.

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References

Akiskal, H. S. (1982) Factors associated with incomplete recovery in primary depressive illness. *Journal of Clinical Psychiatry*, **43**, 266–271.

—— (1983*a*) Diagnosis and classification of affective disorders: new insights from clinical and laboratory approaches. *Psychiatric Developments*, **2**, 123–160.

—— (1983*b*) The bipolar spectrum: new concepts in classification and diagnosis. In *Psychiatry Update: the American Psychiatric Association Annual Review*, Vol. 2 (ed. L. Grinspoon). Washington, DC: American Psychiatric Press.

——, Walker, P. W., Puzantian, V. R., *et al* (1983) Bipolar outcome in the course of depressive illness: phenomenologic, familial and pharmacological predictors. *Journal of Affective Disorders*, **5**, 115–128.

—— & Mallya, G. (1987) Criteria for the soft bipolar spectrum: treatment implications. *Psychopharmacology Bulletin*, **23**, 68–73.

American Psychiatric Association (1987) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn, revised). Washington, DC: American Psychiatric Press.

Andreasen, N. C., Endicott, J., Spitzer, R. L., *et al* (1977) The family history method using diagnostic criteria. *Archives of General Psychiatry*, **34**, 1229–1235.

Angst, J. (1966) Zur atiologie und nosologie endogener depressiver psycosen. *Monographien aus dem Gesamtgebiete der Neurologie und Psychiatrie*, **112**, 1–118. Berlin: Springer Verlag.

Blazer, O. & Williams, C. D. (1980) Epidemiology of dysphoria and depression in an elderly population. *American Journal of Psychiatry*, **137**, 439–444.

Busse, E. W. & Blazer, D. G. (1980) Disorders related to biological functioning. *Handbook of Geriatric Psychiatry*. New York: Van Nostrand Reinhold.

Cassano, G. B., Musetti, L., Perugi, G., *et al* (1987) Major depression subcategories: their potentiality for clinical research. Diagnosis and treatment of depression. In *Diagnostic et Traitement de la Dépression* (eds K Biziére, S. Garattini & P. Simon). Montpellier: Sanofi Recherche.

Ciompi, L. (1969) Follow-up studies in the evolution of former neurotic and depressive states. *Journal of Geriatric Psychiatry*, **3**, 90–106.

Coryell, W., Endicott, J., Andreasen, N., *et al* (1985) Bipolar I, bipolar II, and nonbipolar major depression among the relatives of affectively ill probands. *American Journal of Psychiatry*, **142**, 817–823.

Depeu, R. A. & Monroe, S. M. D. (1978) The unipolar–bipolar distinction in the depressive disorders. *Psychological Bulletin*, **85**, 1001–1009.

Derogatis, L. R., Lipman, R. S. & Rickels, S. K. (1973) The Hopkins Symptoms Checklist (HSCL): a measure of primary symptoms dimensions in psychological measurement. In *Modern Problems Pharmacopsychiatry* (ed. P. Pichot). Basel: Karger.

Finlayson, R. E. & Martin, L. M. (1982) Recognition and management of depression in the elderly. *Mayo Clinic Proceedings*, **57**, 115–120.

Glasser, M. & Rabins, P. (1984) Mania in the elderly. *Age and Aging*, **13**, 210–213.

Goldfarb, A. I. (1967) Masked depression in the old. *American Journal of Psychotherapy*, **21**, 791–803.

Goldstein, S. E. (1979) Depression in the elderly. *Journal of American Geriatric Society*, **27**, 38–42.

Gurland, B. (1976) The comparative frequency of depression in various adult age groups. *Journal of Gerontology*, **31**, 283–292.

Hamilton, M. (1967) Development of a rating scale for primary depressive illness. *British Journal of Social Clinical Psychology*, **6**, 278–296.

Hopkinson, G. E. & Ley, P. (1969) A genetic study of affective disorder. *British Journal of Psychiatry*, **115**, 917–922.

JACOBY, R. J., LEVY, R., & BIRD, J. M. (1981) Computed tomography and the outcome of affective disorders: a follow-up study of patients. *British Journal of Psychiatry*, **139**, 288–292.

KATON, W. (1982) Depression: somatic symptoms and medical disorders in primary care. *Comprehensive Psychiatry*, **23**, 274–287.

KUKULL, W. A., KOEPSELL, T. D., INUI, T. S., *et al* (1986) Depression and physical illness among elderly general medical clinic patients. *Journal of Affective Disorders*, **10**, 153–162.

MENDLEWICZ, J. (1976) The age factor in depressive illness: some genetic considerations. *Journal of Gerontology*, **31**, 300–303.

MURPHY, E. (1982) Social origins of depression in old age. *British Journal of Psychiatry*, **141**, 135–142.

—— (1983) The prognosis of depression. *British Journal of Psychiatry*, **142**, 111–119.

NIELSEN, A. C. & WILLIAMS, T. A. (1980) Depression in ambulatory medical patients: prevalence by self report questionnaire and recognition by nonpsychiatric physicians. *Archives of General Psychiatry*, **37**, 999–1004.

PICHOT, P. & PULL, C. (1981) Is there an involutional melancholia? *Comprehensive Psychiatry*, **22**, 2–10.

PLACIDI, G. F., RAMPELLO, E. & CASSANO, G. B. (1984) La depressione nell'età senile: aspetti clinici e terapeutici. *Quaderni Italiani di Psichiatria*, **III**, 3–36.

POST, F. (1987) Depression, alcoholism, and other functional syndromes. In *Psychogeriatrics – an International Handbook* (ed. M. Bergener). New York: Springer Publishing Company.

ROTH, M. (1976) The psychiatric disorders of later life. *Psychiatric Annals*. **6**, 57–101.

SALTZMAN, C. & SHADER, R. I. (1978) Depression in the elderly – I. Relationship between depression, psychologic defense mechanism and physical illness. *Journal of American Geriatric Society*, **26**, 253–260.

SCHNEIDER, K. (1958) *Psychopathic Personalities* (trans. by M. W. Hamilton). London: Cassell.

SHAMOIAN, C. A. (1985) Assessing depression in elderly patients. *Hospital and Community Psychiatry*, **36**, 338–339.

SHULMAN, K. & POST, F. (1980) Bipolar affective disorder in old age. *British Journal of Psychiatry*, **136**, 26–32.

STEUER, J., BANK, L., OLSEN, E. J., *et al* (1980) Depression, physical health, and somatic complaints in the elderly: a study of the Zung Self-Rating Depression Scale. *Journal of Gerontology*, **35**, 683–688.

WIDLÖCHER, D. (1983) Psychomotor retardation: clinical, theoretical, and psychometric aspects. *Psychiatric Clinics of North America*, **6**, 27–40.

WINOKUR, G., MORRISON, J., CLANCY, J., *et al* (1973) The Iowa 500: familial and clinical findings favor two kinds of depressive illness. *Comprehensive Psychiatry*, **14**, 99–107.

——, BEHAN, D. & SCHLESSER, M. (1980) Clinical and biological aspects of depression in the elderly. In *Psychopathology in the Aged* (eds J. O. Cole & J. E. Barrett). New York: Raven Press.

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Socio-Cultural Parameters in Yoruba Nigerian Patients with Affective Disorders

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One hundred and ten consecutive new patients presenting with major affective disorders were divided into five categories according to pattern of presentation: recurrent manic disorder, recurrent depressive disorder, bipolar disorder, single episodes of manic disorder, and single episodes of major depressive disorder. Manic patients predominated, and recurrent manic disorder was much more frequent than either recurrent depressive or bipolar disorder. The manic and bipolar patients were younger. Females predominanted in all five groups of patients. The two manic groups were less likely to be married, but this was probably a reflection of their younger age. No differences were demonstrated with regard to educational status or occupation. There were no significant differences with regard to sibship position, family size, or polygamous/monogamous parents. Manic patients were more likely to have suffered permanent separation from one or both parents before the age of 12 years. A relatively low proportion of the patients had a positive history of mental disorder among first- or second-degree relatives. Manic and bipolar patients tended to present in hospital relatively early in their illness.

The affective disorders have been well documented as clinical entities in Nigerian populations (Lambo, 1960; Olatawura, 1973; Binitie, 1975; Makanjuola, 1982, 1985), and there are indications that manic illnesses may be more frequent than depressive episodes (Makanjuola, 1986*a*), in contrast to industrialised nations (Winokur *et al*, 1969; Boyd & Weissman, 1981). Similar observations have been made in other non-Caucasian races (see Slater & Roth, 1969; Leonhard, 1986) and even in black immigrants to the United Kingdom (Leff *et al*, 1976). Recently, it has been demonstrated that in the Yoruba Nigerian, "recurrent unipolar manic disorder" is much more common than bipolar disorder (Makanjuola, 1982, 1985). However, it is possible that these findings do not reflect the real situation in the community. Depressive disorders may cause less disruption to the family and to society, and be less likely to present in hospital. Suicide and attempted suicide are relatively uncommon in Nigerians (Asuni, 1965, 1967). Also, depressive disorders in Nigerians are characterised by prominent somatic complaints, which may mask the underlying mental disorder (Olatawura, 1973; Binitie, 1975, 1981; Makanjuola, 1987), leading to possible misdiagnosis and presentation at a non-psychiatric medical facility.

Although these factors may contribute somewhat to the observations on the pattern of presentation of affective disorders in Nigerians, which have mainly been made on hospital populations, it is unlikely that they provide the whole answer, particularly since some of the observations have come from prospective studies (Makanjuola, 1982, 1985). Consideration must therefore be given to the possibility that socio-cultural or biological factors may exert important influences, resulting in a higher proportion of manic as opposed to depressive episodes, and a preponderance of unipolar over bipolar manic disorder. Leonhard (1986) has postulated that the preponderance of manic states in developing countries may be related to larger family size.

There is a need for studies of aetiological factors in affective disorders among the populations of developing countries. Biological studies should include evaluation of central neurotransmitter functions, cellular ion transport mechanisms, cerebral morphology, and genetic factors. Socio-cultural studies should include evaluation of such parameters as sibship position and family size, patterns of upbringing, traumatic events during development, and culturally determined attitudes to losses and other traumas. Transcultural comparative studies would be ideal. A comparison of these variables in different categories of affective disorder in individual cultures should also provide useful information. The present paper describes an evaluation of family and other social parameters in Yoruba Nigerian patients suffering from different forms of affective disorder.

Method

The study took place at the psychiatric unit of the Wesley Guild Hospital, Ilesha, Western Nigeria. The population served by this unit is predominantly rural Yoruba (Makanjuola, 1986*a*). The society is largely traditional, most households are polygamous, and the extended family system operates (Fadipe, 1970; Makanjuola, 1986*b*). Although the majority are nominally Christian or Moslem (Federal Census Office, 1963), the traditional ('Orisha') religion is still influential.

All new Yoruba patients presenting at the psychiatric unit between 1 October 1982 and 30 September 1986, and who met DSM-III (American Psychiatric Association, 1980) criteria for major depressive episode or manic episode, were included in the study (110 in total). Each patient was subjected to a full psychiatric and physical evaluation by the author. Background clinical and social data were collected on a specially designed form, and details of previous episodes of mental disorder obtained. Patients were followed up by the author, and further episodes of mental disorder documented until 30 September 1986. Five categories of mental disorder were defined, taking into consideration the patient's psychiatric history before and after presentation:

(a) recurrent unipolar manic disorder: at least two manic episodes (including the current one), none of major depressive disorder ($n = 30$)
(b) recurrent unipolar depressive disorder: at least two major depressive episodes (including the current one), none of manic disorder ($n = 9$)
(c) bipolar disorder: at least one episode each of mania and of major depressive disorder ($n = 10$)
(d) single manic episode: current manic episode, no other episode of manic or major depressive disorder or of psychosis ($n = 29$)
(e) single depressive episode: current major depressive episode, no other episode of manic or major depressive disorder, or of psychosis ($n = 32$).

There were great problems in obtaining sufficient data to make specific diagnoses for family members with a positive history of psychiatric disorder. A specific DSM-III diagnosis was in most cases possible only when the affected relative was available for interview, or when hospital records were available.

Results

The results are summarised in Table I. The majority of the patients belonged to one of the two manic groups. Recurrent manic disorder was much more common than either bipolar or recurrent depressive disorder. The two manic groups were younger at disease onset and at presentation than the two depressive groups. There was a statistically significant preponderance of females overall, but not between the separate groups. There were no obvious differences in occupation and educational status, or religion, but there were significant differences with regard to marital status, a greater proportion of members of the two manic groups having never been married, but this was probably a result of their younger age.

There were no significant differences with regard to full-sibship position (although it was considered that data obtained on overall sibship position, full as well as half-siblings, might not be accurate) or number of full siblings in the families of the patients. A tendency for the total family size (full plus half-siblings) to be greatest in the two manic groups and lowest in the recurrent depressive group did not achieve statistical significance. The patients had been brought up predominantly in polygamous homes (80% overall), but there were no obvious differences between the five groups. More of the patients in the two manic groups had suffered permanent separation from one or both parents in the first 12 years of life, and when the two manic groups and the two depressive groups were combined, this difference became statistically significant. A relatively low proportion of the patients had a positive family history of mental disorder, usually of affective disorder, and the numbers involved are too small for valid comparisons.

There were significant differences in duration of index episode before presentation, the intervals being lower in the two manic and the bipolar groups. (Most of the bipolar group (nine out of ten) actually presented with a manic episode.) Among the three groups with recurrent disorder there was a tendency for the bipolar patients to have a greater total number as well as frequency of episodes of affective disorder, but this was not statistically significant.

Discussion

In agreement with previous observations (Makanjuola, 1982, 1985, 1986*a*), this study has demonstrated a preponderance of manic over depressive patients among Yoruba Nigerian psychiatric patients, as well as a preponderance of recurrent unipolar manic disorder over bipolar and indeed recurrent depressive disorder.

The data obtained, particularly family data, have been somewhat restricted as a result of personnel limitations. In the interest of accuracy, a deliberate decision was taken to restrict the parameters examined. Nevertheless, it was expected that some differences would be found among the different groups of patients which might yield some indications concerning the reasons underlying the different pattern of presentation of the affective disorders in the Yoruba Nigerian.

There were significant differences in age both at onset of first episode and at index presentation among the five groups, with those of the two manic groups being younger and the two depressive groups older. The relatively younger ages of bipolar compared with unipolar depressives is well established (Winokur *et al*, 1969; Gershon *et al*, 1976). Previous studies have failed to demonstrate significant differences in ages of onset between recurrent unipolar manics and bipolar patients (Abrams *et al*, 1979; Nurnberger *et al*, 1979; Pfohl *et al*, 1982). It should be noted that, as in a previous study (Makanjuola, 1985), the age differences found between patients in the two manic and the bipolar groups were rather small. There were no significant

TABLE I

Comparative data on the five groups of patients[1]

	Patient Group					
	Single depressive episode (n = 32)	*Recurrent depressive disorder* (n = 9)	*Bipolar disorder* (n = 10)	*Recurrent manic disorder* (n = 30)	*Single manic episode* (n = 29)	*Statistical analysis (where appropriate)*
Age at presentation (mean ± s.d.)	35.3 ± 14.5	47.2 ± 17.5	31.2 ± 12.6	26.2 ± 7.5	25.8 ± 8.1	ANOVA: $F = 8.33$, $P < 0.01$
Age at first episode (mean ± s.d.)	34.7 ± 13.8	36.1 ± 15.6	28.1 ± 13.6	21.6 ± 5.0	25.5 ± 8.0	ANOVA: $F = 7.50$, $P < 0.01$
No. of male patients	9	1	4	10	11	$\chi^2 = 2.89$, NS
No of female patients	23	8	6	20	18	
Full-sibship position (mean ± s.d.)	2.7 ± 1.5	1.3 ± 0.5	2.4 ± 1.5	2.4 ± 1.3	2.4 ± 1.4	ANOVA: $F = 1.47$, NS
Number of full siblings (mean ± s.d.)	4.3 ± 1.9	2.6 ± 1.4	4.3 ± 1.8	4.2 ± 2.2	4.5 ± 1.9	ANOVA: $F = 1.77$, NS
Total siblings (full + half) (mean ± s.d.)	9.3 ± 5.5	4.7 ± 1.8	9.5 ± 5.6	11.3 ± 6.8	11.6 ± 9.0	ANOVA: $F = 2.07$, NS
Permanent separation from parent before 12 years of age	2	0	1	8	5	$\chi^2 = 4.32$, $P < 0.05$ (comparison of combined depressive and combined manic groups)
Marital status						
Never married	8	0	4	16	19	$\chi^2 = 18.29$, $P < 0.01$ (never married v. currently plus previously married)
Currently married	21	6	5	8	7	
Divorced/separated/widowed	3	3	1	6	3	
Type of marriage[2]						
Monogamous	18	3	4	10	9	
Polygamous	6	6	2	4	1	
Religion						
Christian	28	5	10	23	22	$\chi^2 = 7.50$, NS
Moslem	4	4	0	7	7	
Duration of current episode (mean ± s.d.): months	8.8 ± 14.00	8.1 ± 12.8	1.4 ± 2.4	2.1 ± 3.6	3.1 ± 2.3	ANOVA: $F = 2.51$, $P < 0.05$
No. of episodes (mean ± s.d.)		3.0 ± 1.6	3.5 ± 1.1	2.7 ± 0.9		ANOVA: $F = 2.05$, NS
Interval between episodes (mean ± s.d.): years		3.6 ± 1.5	1.5 ± 1.2	2.2 ± 2.0		ANOVA: $F = 2.19$, NS

[1] There were no obvious differences in educational and occupational status (data available from author on request).

[2] Refers to currently plus previously married patients.

differences in sex ratio among the different groups, in contrast to previous studies (Perris, 1966; Winokur *et al*, 1969; Gershon *et al*, 1976; Abrams *et al*, 1979; Nurnberger *et al*, 1979; Boyd & Weissman, 1981; Pfohl *et al*, 1982). There was a non-significant trend towards larger overall family size (full plus half-siblings considered) among the two manic groups; thus Leonhard's (1986) expectations were not confirmed.

Interestingly, a history of permanent separation (usually as a result of death) from one or both parents during childhood was more common among the manic patients than among the two depressive groups. The relationship between parental loss in childhood and the later development of affective disorder is controversial. Most of the studies concern depressive disorders, and the findings are variable (see Perris *et al*, 1986); however, some studies have demonstrated a relationship between parental loss and manic or bipolar disorder (Perris & Perris, 1978; Pfohl *et al*, 1983). The psychodynamic concept of the 'manic defence' notwithstanding, it is difficult to account for an excess of parental loss in manic over depressive patients. The finding requires confirmation.

The relatively low frequency of a family history of mental disorder, albeit predominantly of affective disorders, is consistent with previous findings (Makanjuola, 1982, 1985). The author and his coworker have found a similar low frequency of positive family history of mental disorder among patients suffering from schizophrenic and schizophreniform disorders (Makanjuola & Adedapo, 1986). The significantly lower duration of index illness before presentation among the manic and bipolar groups is almost certainly related to the relative acuteness of most manic episodes, and their greater tendency to produce family and social crisis.

In conclusion, the present study has not produced convincing evidence in favour of differences in the particular socio-cultural factors studied. It follows from this that such socio-cultural factors (at least those examined in this study) may not provide explanations for the different patterns of presentation of affective disorder in Yoruba Nigerian patients as opposed to Caucasians. While further studies are indicated, it would appear that attention should also be focused on biological factors.

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References

Abrams, R., Hayman, M. A. & Krishna, V. R. (1979) Unipolar mania revisited. *Journal of Affective Disorders*, 1, 59–68.

Asuni, T. (1965) Suicide in Western Nigeria. *International Journal of Psychiatry*, 1, 52–63.

—— (1967) Attempted suicide in Western Nigeria. *Central African Journal of Medicine*, 13, 289–293.

American Psychiatric Association (1980) *Diagnostic and Statistical Manual of Psychiatric Disorders* (3rd edn) (DSM–III). Washington, DC: APA.

Binitie, A. O. (1975) A factor-analytic study of depression across cultures (African and European). *British Journal of Psychiatry*, 127, 559–563.

—— (1981) The clinical manifestations of depression in Africans. *Psychopathologie Africaine*, 17, 36–40.

Boyd, J. H. & Weissman, M. M. (1981) Epidemiology of affective disorder. *Archives of General Psychiatry*, 38, 1039–1046.

Fadipe, (1970) *The Sociology of the Yoruba Ibadan*. Ibadan: Ibadan University Press.

Federal Census Office (1963) *Population Census of Western Nigeria*. Lagos: Federal Census Office.

Gershon, E. S., Bunney, Q. E., Leckman, J. K., *et al* (1976) The incidence of affective disorders: a review of data and hypotheses. *Behaviour Genetics*, 9, 227–261.

Lambo, T. A. (1960) Further neuropsychiatric observations in Nigeria (with comments on the need for epidemiological study in Nigeria). *British Medical Journal*, *ii*, 1694–1704.

Leff, J. P., Fischer, H. & Bestelson, A. (1976) A cross-national epidemiological study of mania. *British Journal of Psychiatry*, 129, 428–442.

Leonhard, M. (1986) Different causative factors in different forms of schizophrenia. *British Journal of Psychiatry*, 149, 1–6.

Makanjuola, R. O. A. (1982) Manic disorder in Nigerians. *British Journal of Psychiatry*, 141, 456–463.

—— (1985) Recurrent unipolar manic disorder in the Yoruba Nigerian: further evidence. *British Journal of Psychiatry*, 147, 434–437.

—— (1986*a*) Clinical and socio-cultural parameters in Nigerian psychiatric patients. A prospective study. *Acta Psychiatrica Scandinavica*, 72, 512–521.

—— (1986*b*) The Nigerian psychiatric patient and his family. *International Journal of Family Psychiatry* (in press).

—— (1987) "Ode Ori": a culture-bound disorder with prominent somatic features in Yoruba Nigerian patients. *Acta Psychiatrica Scandinavica*, 75, 231–236.

—— & Adedapo, S. A. (1986) The DSM–III concepts of schizophrenia and schizophreniform disorders: a clinical and prognostic evaluation. *British Journal of Psychiatry*, 151, 611–618.

Nurnberger, J., Roose, S. P., Dunner, D. L., *et al* (1979) Unipolar mania: a distinct clinical entity. *American Journal of Psychiatry*, 136, 1420–1423.

Olatawura, M. O. (1973) The problem of diagnosing depression in Nigeria. *Psychopathologie Africaine*, 9, 389–403.

Perris, C. (1966) A study of bipolar manic–depressive and unipolar recurrent depressive psychosis. *Acta Psychiatrica Scandinavica*, 42, (suppl. 194).

—— & Perris, H. (1978) Status within the family and early life experiences in patients with affective disorders and cycloid psychosis. *Psychiatrica Clinica*, 11, 155–162.

——, Holmgren, S., Von Knorring, L., *et al* (1986) Parental loss by death in the early childhood of depressed patients and their healthy siblings. *British Journal of Psychiatry*, 148, 165–169.

Pfohl, B., Vasquez, N. & Nasralla, H. (1982) Unipolar vs bipolar mania: a review of 242 patients. *British Journal of Psychiatry*, 141, 453–458.

——, Stanel, D. & Tsuang, M. T. (1983) The association between early parental loss and diagnosis in the IOWA 500. *Archives of General Psychiatry*, 40, 965–967.

Slater, E. & Roth, M. (1969) *Clinical Psychiatry*. London: Baillière, Tindall and Cassell.

Winokur, G., Clayton, P. & Reich, T. (1969) *Manic–Depressive Illness*. St Louis: Mosby.

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A Study of the Effects of Desipramine Treatment Alone and in Combination with L-Triiodothyronine on 6-Sulphatoxymelatonin Excretion in Depressed Patients

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Urinary 6-sulphatoxymelatonin (αMT6s) excretion was measured after one day and one, two and three weeks of desipramine treatment in eight depressed patients. There was a significant increase in the urinary excretion of αMT6s after one week of treatment, and at no time was there any decrease in αMT6s excretion. These findings are opposed to the hypothesis that desipramine reduces noradrenergic neurotransmission in the human pineal. In a further five patients whose depression was resistant to desipramine alone, urinary αMT6s excretion was measured during treatment with adjunctive L-triiodothyronine (T_3). There was no change in αMT6s excretion, and thus the previously reported potentiation of the efficacy of tricyclic antidepressants in combination with T_3 does not appear to be mediated through an alteration in noradrenergic neurotransmission.

The overall effect of antidepressant drugs on noradrenergic neurotransmission has still not been determined. If, as Sulser and co-workers propose (Sulser *et al*, 1978; Sulser, 1984), the predominant effect of chronic treatment with these drugs is to reduce the sensitivity of post-synaptic β_1 adrenoceptors, then noradrenergic neurotransmission would be reduced. However, if the main effect is inhibition of noradrenaline uptake in combination with downregulation of pre-synaptic α_2 adrenoceptors (Eriksson *et al*, 1982; Heal *et al*, 1983; Plaznik *et al*, 1984) and upregulation of post-synaptic α_1 adrenoceptors (Menkes *et al*, 1983; Plaznik *et al*, 1984), then noradrenergic neurotransmission would be enhanced. Thus studies in animals that examine effects of antidepressant drugs on individual classes of adrenoceptor cannot provide direct evidence for the functional effect of antidepressant drugs on net noradrenergic neurotransmission.

The secretion of melatonin from the pineal gland has been proposed as a model of the overall effect on noradrenergic neurotransmission of antidepressant drugs (Lewy, 1984; Checkley *et al*, 1986). The gland is innervated by noradrenergic fibres which have pre-junctional α_2 adrenoceptors (Pelayo *et al*, 1977) and post-synaptic β_1 adrenoceptors (Zatz *et al*, 1976) and $\alpha_1$adrenoceptors (Vanecek *et al*, 1985), at least in the rat. Although a drug may induce functional changes in one or more of these adrenoceptor populations, an overall increase or decrease in neurotransmission will be reflected by either an increase or decrease in melatonin synthesis.

In animals, chronic treatment with tricyclic antidepressant drugs has been shown to reduce the number of β adrenoceptors in pineal tissue (Cowen *et al*, 1983; Friedman *et al*, 1984). Along with this downregulation at β adrenoceptors has been described a reduced activity of the enzyme N-acetyl transferase (Friedman *et al*, 1984), which regulates the synthesis of melatonin. In some, though not all, studies a corresponding reduction in pineal (Heydorn *et al*, 1982; Friedman *et al*, 1984) and plasma (Heydorn *et al*, 1982) melatonin concentration has also been reported, although some have found no change in nocturnal melatonin secretion (Cowen *et al*, 1983; Burns & Brown, 1984).

Studies of the effect of chronic antidepressant treatment on melatonin secretion in man have yielded conflicting results. Some (Mendlewicz *et al*, 1980; Brown *et al*, 1985; Fraser *et al*, 1986) have found no effect in depressed patients, while others (Thompson *et al*, 1985) have shown a persistent elevation of plasma melatonin after three weeks of treatment.

All these studies have involved the measurement of melatonin in plasma collected at night, often at hourly intervals. The recent development of an assay for the major urinary metabolite of melatonin, 6-sulphatoxymelatonin (αMT6s), which correlates closely with plasma melatonin (Arendt *et al*, 1985; Bojkowski *et al*, 1987), provides a less intrusive and more convenient means of estimating melatonin secretion over a 24-hour period. Sack & Lewy (1986) measured urinary 6-hydroxymelatonin during treatment with desipramine in four depressed patients. We now report on a larger series of depressed patients treated with desipramine, whose clinical course is also detailed.

Several studies suggest that the therapeutic efficacy of a tricyclic antidepressant may be augmented by the addition of L-triiodothyronine (T_3) (Prange *et al*, 1969; Coppen *et al*, 1972; Feighner *et al*, 1972; Wheatley, 1972). Moreover, depressed patients resistant to tricyclic antidepressants alone have improved after the addition of T_3 (Tsutsui *et al*, 1979; Goodwin *et al*, 1982; Schwartz *et al*, 1984), although a more recent double-blind placebo-controlled trial failed to show any therapeutic efficacy of T_3 in adjunct to imipramine (Gitlin *et al*, 1987).

Animal studies have shown that T_3 in combination with desipramine delays the downregulation of β adrenoceptors and accelerates the downregulation of pre-synaptic α_2 adrenoceptors (Mason *et al*, 1987; Heal *et al*, 1987). These effects will enhance noradrenergic neurotransmission. If this were the pertinent mechanism for the antidepressant effect of adjunctive T_3 then we would predict that the addition of T_3 to desipramine treatment would cause an increase in noradrenergic neurotransmission and hence melatonin secretion in depressed patients. We therefore studied αMT6s excretion in five patients who were resistant to treatment with desipramine alone and had T_3 added to their treatment regimen.

In animals, chronic treatment with T_3 or thyroxine (T_4) alters β adrenoceptor function (Heal *et al*, 1987; Mason *et al*, 1987), albeit at much higher doses than used in humans. In order to exclude a direct effect of T_3 upon noradrenergic neurotransmission, we obtained serial measures of αMT6s excretion in a patient with myxoedema in whom replacement treatment with thyroxine was commenced.

Method

Desipramine treatment study

Patients. Eight depressed in-patients, who fulfilled the Research Diagnostic Criteria (Spitzer *et al*, 1978) for major depressive disorder, volunteered to participate in the desipramine (DMI) treatment study. All were aged between 18 and 70 years, and suffered no other psychiatric or physical illnesses, including alcoholism. None had taken psychotropic or other medication, apart from benzodiazepines, for at least three weeks prior to the study. The modified Hamilton Rating Scale for Depression (HRSD; Hamilton, 1967) was used to assess the severity of depression prior to treatment and after one and three weeks of treatment.

Treatment. All patients were treated with 150 mg desipramine daily, a dose which was well tolerated, for three weeks. Plasma desipramine concentrations were measured using gas liquid chromatography after 1, 7 and 21 days of treatment.

Sampling. According to the clinical urgency for starting treatment, we were able to obtain between one and four 24-hour urine collections before starting desipramine. Thereafter, further 24-hour urine collections were made on the first day, and after one, two and three weeks of treatment. Total urine volumes were measured and recorded; then 5 ml aliquots were removed and stored in plain plastic tubes at −25°C for subsequent estimation of urinary αMT6s.

Desipramine and L-triiodothyronine (T_3) treatment study

Patients. Five patients conforming to the same selection criteria as described in the DMI treatment study participated in this study. Two of the patients had also taken part in the DMI treatment study. All had major depressive disorders of sufficient severity to require continuing in-patient care after a minimum of four weeks' treatment with desipramine alone and the use of adjunctive therapy was clinically indicated. The patients scored at least 14 on the HRSD. None was taking any other medication apart from benzodiazepines.

Treatment. On day 1 of the study, L-triiodothyronine was added to the desipramine treatment regimen: 20 μg of T_3 was administered daily in divided doses. After one week the daily dose of T_3 was increased to 40 μg and the treatment continued for a further three weeks. In three of the patients the dose of T_3 was reduced to 20 μg daily for the following week before being discontinued completely, on the 42nd day of the study.

Sampling. Serial 24-hour urine collections were made prior to and throughout the period of treatment with DMI and T_3. As far as possible, collections were made daily. Total urine volumes were measured and 5 ml aliquots removed and stored in plain plastic tubes at −25°C for subsequent estimation of urinary αMT6s.

Venous blood samples were taken at weekly intervals for estimation of thyroid-stimulating hormone (TSH), plasma T_4 and free T_4, and also plasma desipramine concentrations.

Clinical measures. The severity of depression was assessed prior to the study and at weekly intervals during the study, using the modified HRSD. The patients were weighed weekly and their pulse rates were measured daily, prior to the morning dose of T_3.

Thyroxine treatment study

A 36-year-old Malaysian woman with an eight-year history of paranoid schizophrenia presented with a two-year history of lethargy, hoarseness, weight gain, dry skin, facial puffiness and cold-intolerance. On examination, she was obese, with dry skin and hair and a coarse facies. She had a bradycardia and slow-relaxing reflexes. The clinical diagnosis of hypothyroidism was confirmed biochemically: serum total thyroxine was 1.2 nmol/1, free thyroxine 1.3 pmol/l and TSH 106 mU/1. There were high titres of thyroid cytoplasmic and thyroglobulin autoantibodies.

Treatment was started with 50 µg thyroxine daily for one week, increased to 100 µg for the second week, and then further increased to a maintenance dose of 150 µg daily. The patient's long-term medication (trifluoperazine 10 mg b.d. and orphenadrine 50 mg t.d.s.) continued unchanged initially, but on the 27th day of treatment, trifluoperazine was reduced to 15 mg daily.

Serial 24-hour urine collections were made for two days before thyroxine was started, and then made daily for the first 14 days of treatment. Thereafter, 2–3 24-hour urine collections were made weekly for a further four weeks. Specimens for estimation of urinary αMT6s were collected and stored as previously described. Thyroid function was measured after two weeks and six weeks of treatment.

Sulphatoxymelatonin assay

Urinary αMT6s excretion was estimated by radioimmunoassay (Arendt *et al*, 1985). Coefficients of variation inter-assay were 13.9%, 9.9% and 14% at 2.9 ng/ml, 8.3 ng/ml and 20.9 ng/ml urine respectively. Intra-assay coefficients of variation were 6.5%, 3.3% and 4.1% at 2.5 nl/ml, 12 ng/ml and 28.3 ng/ml respectively. The assay limit of detection was 0.65 ng αMT6s per millilitre of urine.

Statistical analysis

Because of the small sample size, normality of distribution could not be assumed, and so αMT6s data in the desipramine treatment study was analysed using the Wilcoxon signed-rank test, for each time point studied. To analyse treatment effect, independent of time, the αMT6s data obtained at all time points after treatment was collapsed down to a single mean and compared with αMT6s excretion before treatment using the Wilcoxon signed-rank test.

Results

Desipramine treatment study

Four male and four female patients participated in the DMI treatment study. They had a mean age of 50 years (range 29–69 years), a mean weight of 63.2 kg (range 48–80 kg) and a mean height of 169 cm (range 156–180 cm). The mean pre-treatment score on the HRSD was 23 (range 15–31). After one week of desipramine treatment the score was 19 (range 7.5–24) and after three weeks it was 14 (range 4–26). A statistically significant reduction in Hamilton score was reached after three weeks of treatment ($P<0.05$, 2-tailed paired *t*-test).

During the study, four patients were also treated with a benzodiazepine hypnotic, three receiving 20 mg temazepam and one 10 mg nitrazepam.

Plasma desipramine concentrations. After one day of treatment, mean plasma DMI concentration was 48 (s.e.m. 29) µg/l. After one week and three weeks, mean plasma levels were 84 (s.e.m. 25) µg/l and 137 (s.e.m. 55) µg/l respectively.

Urinary sulphatoxymelatonin. The mean 24-hour excretions of αMT6s during the course of desipramine treatment are shown in Fig. 1. There is a significant increase in αMT6s excretion after one week of treatment ($P<0.005$, Wilcoxon signed-rank test). The mean of all the estimates of αMT6s after desipramine treatment was also significantly greater than mean αMT6s before treatment ($P<0.05$, Wilcoxon signed-rank test).

Desipramine and L-triiodothyronine treatment study

Four male patients and one female patient entered the DMI and T_3 treatment study, but one male was withdrawn after 11 days of treatment because of increasing agitation and delusions which required and later responded to electroconvulsive therapy. We therefore excluded this patient from the data analysis, although his urinary αMT6s secretion levels during the time he remained in the study are depicted in Fig. 2.

The patients had a mean age of 55.6 years (range 44–62), a mean weight of 74 kg (range 60–90 kg) and a mean height of 176 cm (range 160–188 cm).

Three of the four patients who completed the study were not treated with benzodiazepines at any point. The remaining patient received 20 mg temazepam at night on a regular basis. (The patient who was unable to complete the study was receiving 5 mg diazepam nightly.)

Clinical measures. All the patients lost weight during the period of treatment with T_3, and three of the four patients who completed the treatment regained weight the following week (Table I). Weight loss was statistically significant after one, two and three weeks of treatment ($P<0.05$, $P<0.01$, and $P<0.02$ respectively, 2-tailed paired *t*-test).

Depressive symptoms improved clinically in one patient; in the remaining three who completed the treatment there was no clinical benefit. Four patients complained of

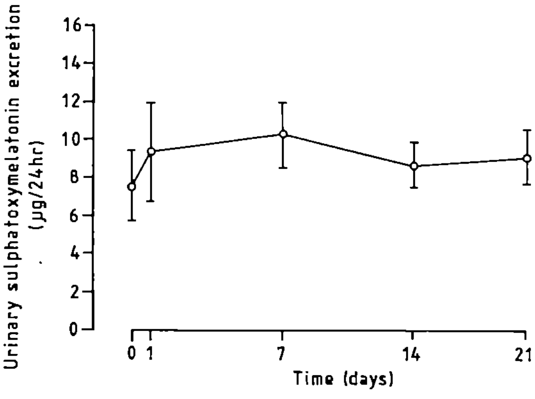

FIG. 1 Mean 24-hour urinary 6-sulphatoxymelatonin excretion (±s.e.m.) for eight depressed patients prior to and during treatment with desipramine.

TABLE I

Clinical measures and thyroid-function status of four depressed patients during treatment with desipramine and T_3

	Treatment time						
	0 days	*7 days*	*14 days*	*21 days*	*28 days*	*35 days*	*42 days*
Daily dose T_3: μg	0	20	40	40	20	0	0
Weekly pulse: min^{-1}							
Mean	80	89	90	91	91	91	82
Range	70–86	85–93	79–96	77–98	80–99	87–93	79–88
Weight: kg							
Mean	74.4	73.6	72.7	72.1	72.1	72.2	72.8
Range	60.0–90.0	59.0–88.9	58.0–88.0	57.0–87.4	56.5–89.7	56.0–91.0	56.6–93.0
HRSD							
Mean	19	18	16	18	16	16	19
Range	13.5–26.5	12.5–30	3–32.5	4–32.5	3.5–27	8–29	4–28
TSH: mUl							
Mean	3.1	0.7	0.2	0.1	0.1	–	–
Range	0.7–6.5	0.2–1.2	0.1–0.2	0.1–0.1	0.1–0.1	–	–
Thyroxine: nmol/l							
Mean	92	80	60	57	62	–	–
Range	79–105	61–95	47–77	39–74	39–84	–	–
Free T_4 pmol/l							
Mean	17	14	11	10	10.5	–	–
Range	14–22	10.5–19.5	7.5–16	6–15	5.5–15.5	–	–

worsening anxiety, sweating and tremor of the hands; these all improved as soon as the T_3 was stopped. There was an increase in pulse rate in all the patients, which was statistically significant after one and two weeks ($P<0.05$ and $P<0.02$ respectively, 2-tailed paired *t*-test) but not after subsequent weeks.

Plasma desipramine concentrations. The addition of T_3 to the desipramine treatment had no effect on plasma desipramine levels. Before T_3 was started, mean plasma DMI concentration was 155 μg/l (range 24–375 μg/l). Subsequent mean weekly plasma DMI concentration ranged from 143 μg/l (week 3 of T_3 treatment) to 171 μg/l (week 2 of treatment).

Thyroid function. The mean concentration of total thyroxine, free thyroxine and thyroid-stimulating hormone (TSH) levels are shown in Table I. TSH was partially suppressed at a dose of 20 μg T_3 and fully suppressed when the dose was increased to 40μg. There was a concomitant fall in total T_4 and free T_4 concentrations.

Urinary sulphatoxymelatonin. The serial measures of αMT6s excretion in each patient are shown in Fig. 2. Excretion of αMT6s was not influenced by the addition of either 20 μg T_3 to desipramine treatment, or by its subsequent withdrawal.

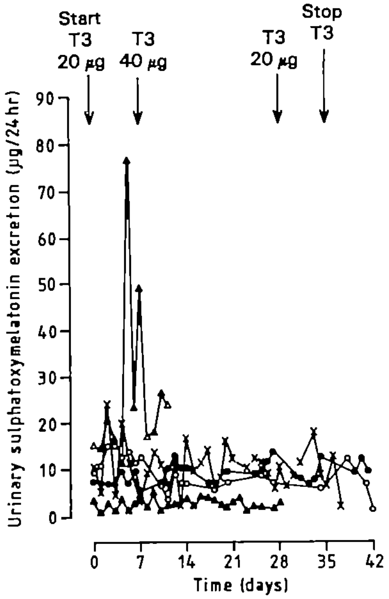

FIG. 2 Serial 24-hour urinary 6-sulphatoxymelatonin excretion for five depressed patients treated with desipramine in combination with L-triiodothyronine (T_3).

Thyroxine treatment study

Efficacy of treatment. After six weeks of treatment with thyroxine, the patient had shown marked clinical improvement. She was more active and alert, her facies was considerably less coarse and puffy and she had lost 5.7 kg in weight.

After two weeks of treatment, serum thyroxine was 70 nmol/l, free T_4 18 pmol/l, and TSH still slightly elevated at 9.7 mU/l. The adequacy of treatment was

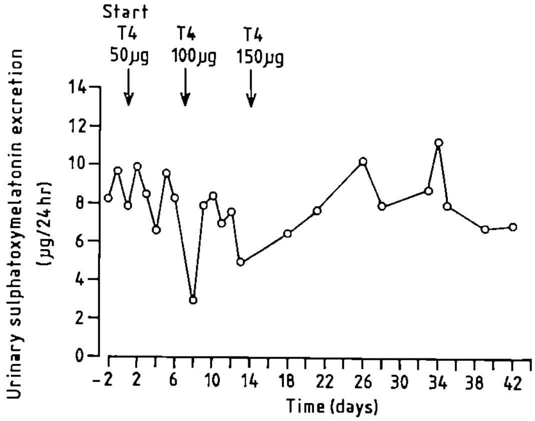

FIG. 3 Serial 24-hour urinary 6-sulphatoxymelatonin excretion in a hypothyroid patient during the introduction of thyroxine (T_4) replacement therapy.

confirmed biochemically after six weeks, all thyroid-function tests being within the normal range (serum total T_4 71 nmol/l, free T_4 22 pmol/l, and TSH 0.4 mU/l).

Urinary αMT6s. Serial measures of αMT6s excretion are shown in Fig. 3. Prior to treatment, αMT6s excretion was within the normal range, and the introduction of increasing doses of thyroxine had no effect on αMT6s excretion.

Discussion

In the present study, αMT6s excretion has been measured as an indicator of the output of the noradrenergic innervation of the human pineal. The hypothesis that antidepressant drugs reduce noradrenergic neurotransmission (Sulser, 1984) predicts that desipramine treatment will reduce αMT6s excretion. No such reaction has been found in our study; on the contrary, αMT6s excretion was significantly increased after one week of treatment with desipramine.

Sack & Lewy (1986), in a study of four depressed patients treated with DMI, found increased urinary 6-hydroxymelatonin after one week; however, they found that the metabolite remained elevated during the second and third weeks of treatment. Golden *et al* (1988) also reported a slight effect of 3–6 weeks of desipramine treatment on 6-hydroxymelatonin excretion. Thompson *et al* (1985) measured nocturnal plasma melatonin concentrations in depressed patients during treatment with DMI, and demonstrated an increase in plasma melatonin after three weeks of treatment, but not after one week. Our results concur with those of Brown *et al* (1985) and Fraser *et al* (1986) who also found no change in plasma melatonin after four weeks of DMI treatment in depressed patients, and Cowen *et al* (1985) who, in a study of chronic DMI treatment in normal volunteers, found an increase in plasma melatonin after 4 and 7 days, but not after 19 days of treatment. Thus although most groups have reported that desipramine enhances melatonin secretion at some stage during treatment, further studies are needed to define the time course of this effect, which may differ between patients and controls and which may be different for plasma melatonin and for urinary αMT6s, although it has been shown that there is a close correlation between plasma melatonin and urinary αMT6s (Arendt *et al* 1985). Since intraindividual urinary αMT6s excretion rates are consistent over time (Bojkowski *et al*, 1987), it is likely that the differences detected in this study are due to the effects of treatment rather than endogenous variation in melatonin secretion rates.

The measurement of αMT6s in the urine rather than melatonin in repeated venous blood samples is less obtrusive for the patient but may provide a less sensitive measure of pineal activity. It is difficult to ensure that patients have provided complete urine collections, particularly at the outset of the study when depressive symptoms are most intense and may compromise compliance. Although consistent within-subject urine volumes were obtained during the study, in future studies it would be useful to measure the ratio of the αMT6s to creatine urinary excretion rates to corroborate the reliability of the urine collections.

Despite some inconsistencies in the results of human studies, no group has reported that DMI reduces melatonin secretion of excretion in man, in contrast to the results from animal experiments (Heydorn *et al*, 1982; Friedman *et al*, 1984). Thus our study provides additional evidence against the hypothesis that antidepressant drugs act by reducing noradrenergic neurotransmission, at least in the human pineal (Sulser *et al*, 1978; Sulser, 1984).

In our series of five depressed patients resistant to DMI treatment, the use of adjunctive T_3 had no effect on the excretion of αMT6s. Thus, despite the influence of T_3 on DMI-induced changes in noradrenergic adrenoceptor function in animals (Heal *et al*, 1987; Mason *et al*, 1987), any changes that may occur in depressed patients are not of sufficient magnitude to alter noradrenergic neurotransmission. Although both in animal models of depression (Brochet *et al*, 1987) and in human studies, a therapeutic effect of T_3 in conjunction with a tricyclic antidepressant has been described, our study suggests that this is unlikely to be mediated through changes in noradrenergic neurotransmission.

Mason *et al* (1987) treated rats with high doses of T_3 or T_4 for seven days and found increased numbers of cortical β adrenergic adrenoceptors. Heal *et al* (1987) found that a single dose of T_3 caused a 25% reduction in cortical β adrenergic adrenoceptors 24 hours later. Joffe *et al* (1988) treated rats with physiological rather than pharmacological doses of T_4 and T_3 and found no effect on β adrenergic adrenoceptors. In our study of a myxoedematous patient embarking on thyroxine replacement therapy, we could expect any enhancement of β adrenergic adrenoceptor function to be reflected by increased melatonin secretion and αMT6s excretion. The fact that there was no change in αMT6s excretion during treatment concurs with Joffe's evidence that physiological doses of T_4 do not influence β adrenergic function.

The concurrent administration of benzodiazepines may have attenuated the effect of desipramine on αMT6s excretion. McIntyre *et al* (1988) have shown that the nocturnal secretion of melatonin was suppressed when four healthy volunteers were treated with alprazolam (1 mg orally) at 9 p.m. We have also found a small but not statistically significant reduction in plasma melatonin concentrations when six healthy volunteers were given diazepam (10 mg i.v.) at 9 p.m. (Checkley *et al*, unpublished data). However, in the present study the doses of benzodiazepines were equivalent to a smaller dose of alprazolam (0.5 mg), which had almost no effect on melatonin (McIntyre *et al*, 1988). If use of benzodiazepines had affected the results of the desipramine study, it would have reduced the effect of desipramine on αMT6s. In the case of the DMI and T_3 study, it is unlikely that benzodiazepine use affected the results since three of the four patients who completed the study took no benzodiazepines.

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References

Arendt, J., Bojkowski, C., Franey, C., *et al* (1985) Immunoassay of 6-hydroxymelatonin sulphate in human plasma and urine: abolition of the urinary 24-hour rhythm with atenolol. *Journal of Clinical Endocrinology and Metabolism*, 60, 1166–1173.

Bojkowski, C., Arendt, J., Shih, M., *et al* (1987) Melatonin secretion in humans assessed by measuring its metabolite: 6-sulfatoxymelatonin. *Clinical Chemistry*, 33, 1343–1348.

Brochet, D. M., Martin, P., Soubrie, P., *et al* (1987) Triiodothyronine potentiation of antidepressant-induced reversal of learned helplessness in rats. *Psychiatry Research* 21, 267–275.

Brown, R. P., Caroff, S., Kocsis, J. H., *et al* (1985) Nocturnal serum melatonin in major depressive disorder before and after desmethylimipramine treatment. *Psychopharmacology Bulletin*, 21, 579–581.

Burns, T. G. & Brown, G. M. (1984) The effects of acute and chronic desmethylimipramine treatment on pineal and serum melatonin and N-acetylserotonin. *Advances in the Biosciences*, 53, 25–30.

Checkley, S. A., Corn, T. H., Glass, I. B., *et al* (1986) Neuroendocrine and other studies of the mechanism of antidepressant action of desipramine. In *Antidepressants and Receptor Function* (CIBA Foundation Symposium 123), pp. 126–147. Chichester: Wiley.

Coppen, A., Whybrow, P. C., Noguera, R., *et al* (1972) The comparative antidepressant value of L-tryptophan and imipramine with and without attempted potentiation by Liothyronine. *Archives of General Psychiatry*, 26, 234–241.

Cowen, P. J., Fraser, S., Grahame-Smith, D. G., *et al* (1983) The effect of chronic antidepressant administration on beta-adrenoceptor function of the rat pineal. *British Journal of Pharmacology*, 78, 89–96.

——, Green, A. R., Grahame-Smith, D. G., *et al* (1985) Plasma melatonin during desmethylimipramine treatment: evidence for changes in noradrenergic transmission. *British Journal of Clinical Pharmacology*, 19, 799–805.

Eriksson, E., Eden, S. & Modigh, K. (1982) Up and down-regulation of central post-synaptic $alpha_2$ adrenoceptors reflected in the GH response to clonidine in reserpine pretreated rats. *Psychopharmacology*, 77, 327–331.

Feighner, J. P., King, L. J., Schuckit, M. A., *et al* (1972) Hormonal potentiation of imipramine and ECT in primary depression. *American Journal of Psychiatry*, 128, 1230–1238.

Frazer, A., Brown, R., Kocsis, J., *et al* (1986) Patterns of melatonin rhythms in depression. *Journal of Neural Transmission* (suppl.) 21, 269–290.

Friedman, E., Yocca, F. D. & Cooper, T. B. (1984) Antidepressant drugs with varying pharmacological profiles alter rat pineal beta adrenergic mediated function. *Journal of Pharmacology and Experimental Therapeutics*, 228, 545–549.

Gitlin, M. J., Weiner, H., Fairbanks, L., *et al* (1987) Failure of T3 to potentiate tricyclic antidepressant response. *Journal of Affective Disorders*, 13, 267–272.

Golden, R. N., Markey, S. P., Risby, E. D., *et al* (1988) Antidepressants reduce whole body norepinephrine turnover while enhancing 6-hydroxymelatonin output. *Archives of General Psychiatry*, 45, 150–154.

Goodwin, F. K., Prange, A. J., Post, R. M., *et al* (1982) Potentiation of antidepressant effects by L-triiodothyronine in tricyclic nonresponders. *American Journal of Psychiatry*, 139, 34–38.

Hamilton, M. (1967) Development of a rating scale for primary depressive illness. *British Journal of Social and Clinical Psychiatry*, 6, 278–296.

Heal, D. J., Lister, S., Smith, S. L., *et al* (1983) The effects of acute and repeated administration of various antidepressant drugs on clonidine-induced hypoactivity in the rat. *Neuropharmacology*, 22, 983–992.

——, Bristow, L. J., Elliot, J. M., *et al* (1987) The influence of L-triiodothyronine (T_3) on the effects of repeated administration of desipramine or electroconvulsive shock on $alpha_2$- and beta-adrenoceptor function in the brain of the rat: implications for the potentiation of antidepressant therapy by T_3. *Neuropharmacology*, 26, 1131–1139.

Heydorn, W. E., Brunswick, D. J. & Frazer, A. (1982) Effect of treatment of rats with antidepressants on melatonin concentrations in the pineal gland and serum. *Journal of Pharmacology and Experimental Therapeutics*, 222, 534–543.

Joffe, R. T., Post, R. M., Sulser, F., *et al* (1988) Effects of thyroid alterations and carbamazepine on cortical beta-adrenergic receptors in the rat. *Neuropharmacology*, 27, 171–174.

Lewy, A. J. (1984) Human melatonin secretion: a marker for adrenergic function. In *Neurobiology of Mood Disorders* (eds R. V. Post & J. C. Ballenger), pp. 207–214. Baltimore: William and Wilkins.

MASON, G. A., BONDY, S. C., NEMEROFF, C. B., *et al* (1987) The effects of thyroid state on beta-adrenergic and serotonergic receptors in rat brain. *Psychoneuroendocrinology*, **12**, 261–270.

MCINTYRE, I. M., BURROWS, G. D. & NORMAN, T. R. (1988) Suppression of plasma melatonin by a single dose of the benzodiazepine alprazolam in humans. *Biological Psychiatry*, **24**, 105–108.

MENDLEWICZ, J., BRANCHEY, L., WEINBERG, U., *et al* (1980) The 24 hour pattern of plasma melatonin in depressed patients before and after treatment. *Communications of Psychopharmacology*, **4**, 49–55.

MENKES, D. B., AGHAJANIAN, G. K. & GALLAGHER, D. W. (1983) Chronic antidepressant treatment enhances agonist affinity of brain alpha$_1$ adrenoceptors. *European Journal of Pharmacology*, **87**, 35–41.

PELAYO, F., DUBOCOVICH, M. L. & LANGER, S. Z. (1977) Regulation of noradrenaline release in the rat pineal through a negative feedback mechanism mediated by presynaptic alpha adrenoceptors. *European Journal of Pharmacology*, **45**, 317–318.

PLAZNIK, A., DANYSZ, W. & KOSTOWSKI, W. (1984) Behavioural evidence for alpha$_1$ adrenoceptor up- and alpha$_2$ adrenoceptor down- regulation in the rat hippocampus after chronic desipramine treatment. *European Journal of Pharmacology*, **101**, 305–306.

PRANGE, A. J., WILSON, I. C., RABON, A. M., *et al* (1969) Enhancement of imipramine antidepressant activity by thyroid hormone. *American Journal of Psychiatry*, **126**, 39–50.

SACK, R. L. & LEWY, A. J. (1986) Desmethylimipramine treatment increases melatonin production in humans. *Biological Psychiatry*, **21**, 406–410.

SCHWARTZ, G., HALARIS, A., BAXTER, L., *et al* (1984) Normal thyroid function in desipramine nonresponders converted to responders by the addition of L-triiodothyronine. *American Journal of Psychiatry*, **141**, 1614–1616.

SPITZER, R. L., ENDICOTT, J. & ROBINS, E. (1978) Research Diagnostic Criteria: rationale and reliability. *Archives of General Psychiatry*, **35**, 773–782.

SULSER, F. (1984) Regulation and function of noradrenaline receptor systems in brain: psychopharmacological aspects. *Neuropharmacology*, **23**, 255–261.

SULSER, F., VETULANI, J. & MOBLEY, P. L. (1978) Mode of action of antidepressant drugs. *Biochemical Pharmacology*, **27**, 257–261.

THOMPSON, C., MEZEY, G., CORN, T. H., *et al* (1985) The effect of desipramine upon melatonin and cortisol secretion in depressed and normal subjects. *British Journal of Psychiatry*, **147**, 389–393.

TSUTSUI, S., YAMAZAKI, Y., NAMBA, T., *et al* (1979) Combined therapy of T$_3$ and antidepressants in depression. *Journal of International Medical Research*, **7**, 138–146.

VANECEK, J., SUGDEN D., WELLER, J., *et al* (1985) Atypical synergistic alpha$_1$ and beta adrenergic regulation of cyclic AMP and cyclic GMP in rat pinealocytes. *Endocrinology*, **116**, 2167–2173.

WHEATLEY, D. (1972) Potentiation of amitriptyline by thyroid hormone. *Archives of General Psychiatry*, **26**, 229–233.

ZATZ, M., KEBABIAN, J. W., ROMERO, J. A., *et al* (1976) Pineal beta adrenergic receptor: correlation of binding of ^{3}H-1-aprenolol with stimulation of adenylate cyclase. *Journal of Pharmacology and Experimental Therapeutics*, **196**, 714–722.

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The Scottish Survey of New Chronic In-patients: Five-Year Follow-Up

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Patients aged 18–64 years, in hospital more than one but less than six years, were followed up five years after identification: 22% had died, 50% remained in-patients, and 28% had been discharged; only 10% of first admissions with organic brain disease had left hospital. Of those discharged, 37% had no contact with after-care services. Of those remaining in hospital, 39% did not require in-patient care. Patients' level of functioning had improved over the five years.

A previous study (McCreadie *et al*, 1983) identified all new chronic in-patients ($n = 571$) on 1 March 1982, in 14 psychiatric hospitals and two general hospital psychiatric units serving 56% of the Scottish population. 'New chronic in-patients' were defined as those aged 18–64 years resident in hospital for more than one but less than six years. There were large differences between hospitals in numbers of such patients (range 12–29 patients per 100 000 general population), and a subsequent survey (McCreadie *et al*, 1985*a*) found marked differences between hospitals in provision of psychiatric rehabilitation and support services. An interim two-year follow-up in 1984 (McCreadie *et al*, 1985*b*) found 71% remained in-patients, 40% of those discharged had no contact with after-care services, and 37% of those remaining in hospital did not require in-patient care. The present study reviews patients' progress five years after the original census, and examines outcome in different hospitals and patient groups.

Method

All hospitals which took part in the original census participated in the follow-up survey (census date 1 May 1987). The hospitals, described elsewhere (McCreadie *et al*, 1983), serve 2.86 million people in a wide range of urban, rural, and mixed catchment areas. The following demographic, hospital, and clinical information, additional to that in the original census, was recorded: whether the patient was alive or dead; marital status; occupational activity; diagnosis; and whereabouts. Some patients had no formal contact with the hospital, but their whereabouts was known, usually by the community psychiatric nurse. For in-patients, the type of ward in which they resided, and their parole and legal status were recorded, and for other patients, their domiciliary status.

In addition, the consultant responsible for each patient, in discussion with other members of the team, assessed rehabilitation status using the Morningside Rehabilitation Status Scale (MRSS; Affleck & McGuire, 1984). This comprises four subscales: dependency, inactivity, isolation, and symptoms; each area is rated on an eight-point scale (0–7), a higher score indicating greater disability. Where patients lived outside hospital, the scale was completed after discussion with relatives and/or community psychiatric nurses. The consultants also indicated where the patient would be best accommodated, and the activity in which he would best be employed, on the assumption that all necessary facilities could be made immediately available in the hospital's catchment area.

Results

By 1987, 22% of the cohort had died, 50% were still in-patients, and contact had been lost with 11%, representing 37% of those discharged from in-patient care (Table I). When domiciliary status was known, 38% of those discharged were living with relatives, a third on their own, and 14% in group homes, proportions similar to those found in 1984. When compared with 1982 results, of those who remained in-patients in 1987 (Table II), fewer were in a closed ward ($\chi^2 = 13.12$, $P < 0.001$) and fewer were

TABLE I
Patients' whereabouts in 1984 and 1987

Whereabouts	*1984* (n = 571) %	*1987* (n = 571) %
Dead	9	22
In-patient, never discharged	67	44
In-patient, discharged but now readmitted	4	6
Day patient	3	6
Out-patient	5	6
Community psychiatric nurse supervision	4	5
No contact	7	8
Whereabouts unknown	1	3

TABLE II
Ward, parole, legal and occupational status of in-patients in 1982, 1984, and 1987

	1982 (n=571) %	*1984* (n=406) %	*1987* (n=283) %
Closed ward	20	9	10
Long-stay or rehabilitation ward	79	84	84
Full parole	56	55	61
Detained under MH(S)A[1] or CP(S)A[2]	18	10	6
No occupation within the hospital	35	40	49
Takes part in occupational or industrial therapy	47	42	36

1. Mental Health (Scotland) Act 1960 or 1984.
2. Criminal Procedure (Scotland) Act 1975.

TABLE III
Patients' accommodation and occupation requirements in 1982, 1984, and 1987

	1982 (n=571) %	*1984*[1] (n=463) %	*1987*[1] (n=379) %
Accommodation			
In-patient	62	55	44
Staffed hostel	20	21	24
Group home	4	7	7
Sheltered lodgings	4	3	6
Own home	6	12	14
Other	4	2	5
Occupation			
Unable to participate	24	29	28
Occupational therapy	32	25	26
Industrial therapy	22	17	13
Sheltered workshop	13	16	22
Open employment	4	5	3
Other	5	8	8

1. Excludes deaths and those not assessed.

detained ($\chi^2=21.69$, $P<0.001$). More in-patients in 1987 when compared with 1982 were not involved in any activities (Table II; 49% v. 35%, $\chi^2=15.11$, $P<0.001$).

In 1982, 44% were diagnosed as schizophrenic, 30% with organic brain disease (including 12% with alcoholic psychosis), 10% as manic-depressive, 6% with personality disorder, and 10% with other diagnoses. By 1987 the diagnosis had been changed from one to another three-digit ICD-9 category (World Health Organization, 1978) in 8% ($n=30$) of those patients remaining alive and in contact with psychiatric services. The diagnosis was changed in 7 of 36 patients originally stated as having a personality disorder (ICD-9, 301).

Fewer patients required hospital in-patient care in 1987 when compared with 1982 and 1984 (Table III; $\chi^2=28.86$ ($P<0.001$), 9.67 ($P<0.01$) respectively). Very similar proportions over the three assessments required staffed hostel accommodation. The requirement for occupational and industrial therapy diminished over the five years ($\chi^2=19.64$, $P<0.001$), while the requirement for sheltered workshops increased ($\chi^2=12.55$, $P<0.001$). As with accommodation, occupation requirements in 1984 lay between those for 1982 and 1987.

Deaths

Over the five years, 126 patients had died. Bronchopneumonia and heart disease accounted for 65%, and 6% were suicides (four were by schizophrenics).

Rehabilitation status

Mean total scores on the MRSS fell over the five years; there was a 12% reduction in dysfunction, which is defined as the score expressed as a percentage of the total score (28). Total scores can also be divided broadly into three groups (Affleck & McGuire, 1984): 0–8, high level of functioning; 9–16, moderate level; and 17 and over, low level; by 1987 51% of those rated were at a moderate or high level of functioning, compared with 29% in 1982. Although there had been improvement in all four subscales between 1982 and 1987, there was little change in isolation and symptom subscales between 1984 and 1987.

TABLE IV
MRSS scores in 356 patients rated on three occasions (1982, 1984, and 1987)

MRSS Scale	*1982*	*1984*	*1987*
Total mean score	19.2*	17.2	16.2**
% dysfunction[1]	69	61	56
Mean scores[2]			
Dependency	6.2*	5.7	5.2***
Inactivity	5.3*	4.7	4.2***
Isolation	4.0*	3.5	3.4
Symptoms	3.7*	3.3	3.4
Range of total scores: %			
0–8 (high)	4	10	16
9–16 (moderate)	24	31	34
17+ (low)	72	59	50

*$P<0.001$, 1982 v. 1984; **$P<0.01$, 1984 v. 1987; ***$P<0.001$, 1984 v. 1987.
1. Score expressed as percentage of maximum score (28).
2. Although mean scores are given, changes over time were measured by the sign test.

356 patients had been assessed on all three occasions by the MRSS (Table IV). There was a continuing improvement over five years; there was a 12% reduction in dysfunction. Also, in 1982, 28% were at a moderate or high level of functioning; by 1987 this figure had risen to 50%. Between 1982 and 1984, and 1984 and 1987 there was a statistically significant improvement in total scores, and scores on dependency and activity subscales (sign tests: P values from <0.01 to <0.001). Between 1982 and 1984 there was a significant improvement in scores on isolation and symptom subscales (sign tests: $P<0.001$) but no significant improvement in either subscale between 1984 and 1987.

Comparisons between groups

Full details, including statistical details, are available on request from RGMcC.

Misplaced patients

In 1982, in the consultants' opinion, 38% of patients were misplaced in hospital. By 1984, 33% of this group had been discharged, a figure rising to 46% by 1987. Only 18% of patients well placed in hospital in 1982 had been discharged by 1987.

Discharged and non-discharged patients

When patients who had been discharged by 1987 were compared with those who had remained in-patients throughout the whole five years, it was found that the former were younger ($P<0.001$), and had at the time of the original census been in hospital a shorter length of time ($P<0.001$). In 1982 more had full parole ($P<0.01$), fewer were in long-stay wards ($P<0.001$), fewer were detained ($P<0.01$), more were schizophrenic ($P<0.02$), fewer required in-patient care ($P<0.001$), and more required sheltered work ($P<0.001$). On the MRSS they were less dependent, more active, less isolated, and had fewer symptoms (all $P<0.001$). In 1987, fewer discharged patients were divorced ($P<0.001$), and more required sheltered work ($P<0.001$). Again, on the MRSS, they were less dependent, more active, less isolated, and had fewer symptoms (all $P<0.001$). In the opinion of the rehabilitation teams, 39% of those who had never been discharged did not require in-patient care.

Comparisons between hospitals

The three hospitals which in 1982 had most 'new chronics' relative to the size of the catchment population were compared with the others ($n=11$). Patients in these 'high occupancy' hospitals in 1987 remained less disabled on the MRSS: they were less isolated ($P<0.01$), had fewer symptoms ($P<0.05$), and more could participate in hospital activities ($P<0.02$).

Hospitals which in 1983 had the widest range of rehabilitation and support services, the 'adequate' hospitals ($n=5$: McCreadie *et al*, 1985*a*), were compared with the others. The rehabilitation status of patients in both groups improved significantly over the five years, and there was no difference in the proportion of patients discharged. A trend, not statistically significant, was that more patients discharged from hospitals with adequate support services were still in contact at follow-up (72% v. 54%).

Discussion

As with the two previous surveys (McCreadie *et al*, 1983, 1985*b*), hospitals serving only 56% of the Scottish population are included. This was simply due to non-response on the part of the other hospitals; we have no reason to believe the remaining 44% comprise a different population structure. This is the first UK study to follow a cohort of 'new chronics' from many different hospitals serving a wide range of catchment areas, over five years, although there have been a small number of studies following up patients from individual hospitals (McCreadie, 1980; Wykes, 1983; Platman & Booker, 1984).

In terms of resettlement, the results make gloomy reading. Five years after identification almost three-quarters of 'new chronics' had died or become 'old chronics'. More than a third of those discharged had lost contact with psychiatric services. Whether these patients had rejected the hospital or vice versa is not clear, although it is noteworthy that more patients discharged from hospitals with 'adequate' rehabilitation and support services (McCreadie *et al*, 1985*a*) remained in contact. Six per cent of deaths were suicides; thus the rate per 100 000 per year in new chronic in-patients was 245, over 15 times that in the general population, which in Scotland in 1986, according to the Registrar General's figures, was 13.7 per 100 000 over the age of 15 years.

On a more optimistic note, patients' rehabilitation status as assessed by the MRSS improved over the five years, and by 1987 half of those rated were at a moderate or high level of functioning. It is noteworthy that although improvement continued between 1984 and 1987 in dependency and inactivity subscales, there was no further improvement in isolation or current symptoms. Change in the latter three years was thus less than in the first two.

Many patients functioning reasonably well remain in hospital. In large part this is probably through lack of suitable alternative accommodation. In the opinion of the rehabilitation teams, a significant minority (20–24%) over the three assessments (1982, 1984, 1987) did not require in-patient care but could live in staffed hostels; such facilities were almost non-existent in Scotland in 1983 (McCreadie *et al*, 1985*a*) and there have been few developments since then.

The type of patient who *was* discharged is not unexpected – the young schizophrenic who in 1982 was less disabled as assessed by the MRSS and had been in hospital a shorter time.

The 1982 survey revealed a wide variation between hospitals in numbers of 'new chronics' relative to the size of the catchment population, thought to be due in part to staff attitudes (McCreadie *et al*, 1983). In 1982 the patients in 'high-occupancy' hospitals were less disabled on the MRSS than those in the other hospitals. This difference was maintained in 1987, although in both groups patients had improved over the five years. In 1982 more patients could have been discharged from low-occupancy hospitals if facilities were available, but in 1987 the proportion of patients that could be discharged was the same in both groups of hospitals, a finding similar to that in 1984. Perhaps clinicians' knowledge of 1982 findings might have altered their assessment of some patients' requirement to be in hospital.

We conclude that 'new chronics' five years after identification remain a disabled population. Many require prolonged in-patient care and thus have become 'old chronics'. The move to 'community care' and the suggested closure of mental hospitals must not be accompanied by a deterioration in services for this group of patients.

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References

AFFLECK, J. W. & MCGUIRE, R. J. (1984) The measurement of psychiatric rehabilitation status: a review of the needs and a new scale. *British Journal of Psychiatry*, **145**, 517–525.

MCCREADIE, R. G. (1980) Clinical and social aspects of long-stay psychiatric patients. *Health Bulletin*, **38**, 70–76.

——, AFFLECK, J. W. & ROBINSON, A. D. T. (1985*a*) The Scottish survey of psychiatric rehabilitation and support services. *British Journal of Psychiatry*, **147**, 289–294.

——, ROBINSON, A. D. T. & WILSON, A. O. A. (1985*b*) The Scottish survey of new chronic inpatients: two year follow-up. *British Journal of Psychiatry*, **147**, 637–640.

——, WILSON, A. O. A. & BURTON, L. L. (1983) The Scottish survey of 'new chronic' inpatients. *British Journal of Psychiatry*, **143**, 564–571.

PLATMAN, S. R. & BOOKER, T. C. (1984) The new long-term patient in the public mental hospital: a follow-up. *American Journal of Psychiatry*, **141**, 794–795.

WORLD HEALTH ORGANIZATION (1978) *Mental Disorders: Glossary and Guide to their Classification in Accordance with the Ninth Revision of the International Classification of Diseases*. Geneva: WHO.

WYKES, T. (1983) A follow-up of 'new' long-stay patients in Camberwell 1977–82. *Psychological Medicine*, **12**, 177–190.

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The Significance of Stupor in the Long-Term Outcome of Chronic Schizophrenia

J. C. RIGBY, S. M. WOOD and R. H. S. MINDHAM

The admission records of 271 long-stay chronic schizophrenic patients, resident in a large psychiatric hospital, were examined in order to identify those who had presented in stupor at the onset of their illness. Twelve patients were found (ten men and two women). When compared, in terms of current mental state and behaviour, with a similar sample of schizophrenics in whom stupor had been absent, significant differences between the two groups were detected, with those presenting in stupor demonstrating a less favourable outcome.

Within the rubric of schizophrenia, stupor is usually classed as a catatonic feature and, along with states of pathological excitement and other motor abnormalities, such as catalepsy, negativism, and echophenomena, was a core component of this subtype when first delineated (Wender, 1963). However, despite their frequently being placed together, stupor does not necessarily always occur in combination with these other features, and it is generally recognised that the stuporose state may be the only catatonic manifestation (Johnson, 1982), while conversely it may be absent in other cases where alternative components are prominent (Abrams & Taylor, 1976); they are thus only partially related (Berrios, 1981). While the outcome of the catatonic subtype of schizophrenia in its entirety has been studied (Bellinger, 1932; Hinsie, 1934; Rupp & Fletcher, 1940; Morrison, 1974*a*) the prognostic significance of stupor alone has not.

Although in the past a relatively common feature of schizophrenia, stupor is now only rarely seen (Joyston-Bechal, 1966; Johnson, 1982) and, along with other catatonic phenomena, its decline is well documented (Achte, 1961; Morrison, 1974*b*; Mahendra, 1981). Nevertheless, schizophrenics who presented in stupor many years ago are still to be found on long-stay wards. The present study was carried out to assess whether, within a group of long-stay schizophrenics, those presenting with stupor had fared differently from those presenting in other ways.

Method

Subjects

The study was carried out on long-stay patients in High Royds Hospital, a large psychiatric hospital in West Yorkshire. The minimum duration of illness for inclusion was 30 years, because after the mid-1950s, the mental state as recorded on admission became much less detailed than previously, and was usually insufficient for the purposes of confirming a diagnosis of schizophrenia according to recognised operational standards (DSM–III; American Psychiatric Association, 1980). The admission records of all patients who qualified with this length of illness were examined to detect those who satisfied DSM–III criteria on admission, had exhibited stupor as one of the presenting features of their illness, and had been in-patients throughout. When necessary, requests were made to other hospitals for the appropriate records. Since, in acute psychotic states, apparent mild clouding of consciousness, self-absorption, perplexity or suspicion may resemble stupor, or at least partial stupor, only unequivocal cases corresponding to total akinesis and mutism were considered, and then only when based on an adequate description of mental state in the case notes. Hence, those described merely as 'mute' or 'stuporose', for example, without any additional information or comment, did not qualify for a positive recording.

The control group was selected by taking the next consecutive sex-matched admission, currently also an in-patient and having been so for the term of their illness, who satisfied DSM–III criteria for schizophrenia, but in whom stupor had been absent.

Assessments

Most patients in both sample and control groups were very deteriorated and handicapped, so that many types of evaluation proved impractical. Assessment was thus restricted to an observer rating scale of current mental state, and an analysis of observed behaviour.

Mental state

This was evaluated using the standardised psychiatric assessment for rating chronic psychotic patients devised by Krawieckia *et al* (1977). This is an observer rating scale, in its complete form consisting of eight variables, each rated on a five-point scale, these being depression, anxiety, flattened affect, psychomotor retardation, delusions, hallucinations, thought disorder, and poverty of speech. For the purposes of this study, delusions, hallucinations, and thought disorder were grouped together and analysed separately as positive symptoms giving a maximum possible score of 12, while emotional blunting, psychomotor retardation, and poverty of speech were similarly combined as negative symptoms. The non-specific variables of anxiety and depression were not rated.

Behaviour

This was assessed using the Current Behavioural Schedule (CBS; Owens & Johnstone, 1980). This is a standardised assessment, completed by JCR, of the patient's behaviour over the previous six months, and is based on an interview with a senior nurse, who must have known the patient for a minimum of this time. The patient's behaviour is assessed in the following eight areas of functioning: social behaviour (encompassing spontaneous contacts, response to approaches, ability to carry out instructions, and general comment on appearance, withdrawal, and usual social habits); activity (as demonstrated by employment, leisure activities, level and nature of activity); presence or absence of excessive overactivity; exhibited abnormal behaviour (hallucinations, delusions, abnormal movements, obsessional activities, thought disorder); antisocial and/or aggressive behaviour; incontinence; stability of behaviour over time; whether or not the patient accepts medication readily. When totalled, the maximum possible score is 49. In accordance with the use of the scale by its authors (Johnstone *et al*, 1985) the last item, relating to medication, has not been included in the total scores, so that for the purposes of this study the maximum attainable is 47, with the higher scores representing the better overall performance. The areas covered by the CBS are broad, encompassing such disparate factors as social skills, psychopathology, and continence, so that similar scores could be achieved by individuals with widely differing behaviour patterns. For this reason, the seven subcategories were analysed separately.

Physical examination

All of the patients were physically examined. Particular attention was given to the central nervous system, although sophisticated testing here, such as the evaluation of neurological 'soft signs', proved impractical, since the deteriorated state of most of the patients precluded the necessary co-operation. Assessments relating to extrapyramidal motor abnormalities were not performed. All patients in both study and control groups had been on long-term neuroleptic drug treatment for the major part of their illness, but because of lack of information, it was not possible to quantify this so as to allow comparisons to be made between groups. Physical examination showed no clear pattern of difference between the two groups. Serological tests for syphilis were performed on all subjects.

Results

Admission records were traced for 271 patients (78%) and 12 cases of unequivocal stupor complying with DSM-III criteria for schizophrenia were identified. Eight further patients were excluded from the study; three non-English-speaking Middle Europeans, two patients initially described as suffering from mental handicap, two having had leucotomy, and one epileptic. A further three cases of stupor were also excluded, since the records of mental state on admission were inadequate for the purposes of confirming a diagnosis of schizophrenia according to DSM-III criteria, although this seemed the most likely diagnosis. Seven controls and all 12 of the stupor cases had had at least one course of electroconvulsive therapy. This was not considered sufficient to exclude them from the study, since there is no evidence of long-term impairment following electroconvulsive therapy (Fraser, 1982). Serological tests for syphilis were negative in all cases.

Characteristics of sample and control groups

The stupor sample comprised ten men and two women, mean age 59.5 (s.d. 5.8) years, with a mean illness duration of 38.4 (s.d. 5.8) years and a mean age of onset of 21.2 (s.d. 3.5) years. The corresponding data for the controls were: mean age 61.6 (s.d. 8.1) years, illness duration 39.1 (s.d. 6.1) years, and age of onset 22.5 (s.d. 5.0) years. There were no significant differences between the groups on these three parameters ($t=0.69$; d.f. $=22$; $P<0.01$; $t=0.76$; d.f. $=22$; $P<0.01$; $t=0.27$; d.f. $=22$; $P<0.01$, respectively).

Mental state

There were no significant differences between stupor and control groups in terms of total scores, with means of 9.5 and 9.75 respectively. However, the mean scores for positive symptoms were significantly different: controls 7.2, stupor 0.8 (Mann-Whitney $U=4$, $P<0.01$; as were those for negative symptoms: controls 2.6, stupor 8.7 (Mann-Whitney $U=15$, $P<0.01$). The distribution of scores for positive and negative symptoms are shown respectively in Figs 1 and 2. Analysis of positive and negative scores against age and illness duration by Spearman's rank-order correlation coefficient showed no significant correlations on any

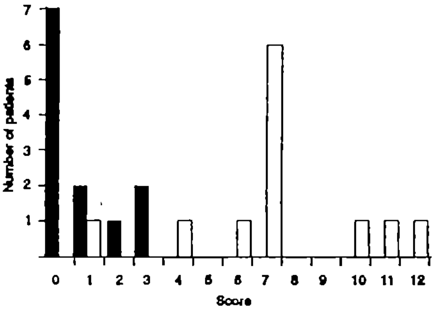

FIG. 1 Distribution of scores for positive symptoms (maximum score = 12) (■ stuporose, □ non-stuporose).

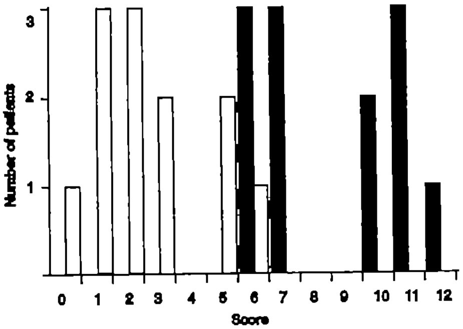

FIG. 2 Distribution of scores for negative symptoms (maximum score = 12) (■ stuporose, □ non-stuporose).

pairings, and although correction for tied ranks revealed a small positive correlation between age and total score for the control group ($Rs=0.58$; $0.05>P>0.01$), it was felt that little weight could be attached to an isolated finding of this nature.

Behaviour

Although the totals on the CBS were similar, significant differences between the two groups were again revealed when the scores of the item groups within the schedule were analysed separately. The controls exhibited better social behaviour (Mann-Whitney $U=7.5$, $P<0.01$), were more active ($U=14$, $P<0.01$), and were less frequently incontinent ($U=22$, $P<0.01$), while the stupor sample had a significantly higher score on the item referring to hallucinations, delusions, obsessional activity, and thought and movement disorder, thus indicating a lesser degree of exhibited abnormal behaviour ($U=12$, $P<0.01$). There were no significant differences on the parameters of antisocial acts or stability of behaviour, and pathological overactivity was absent in all cases. The distribution of scores on the items referring to social behaviour and exhibited abnormal behaviour are shown in Figs 3 and 4 respectively. The patterns seen with the activity and incontinence items are similar, and have therefore not been illustrated. All variables were tested against age and illness duration using Spearman's rank-order correlation coefficient, and no significant correlations were revealed.

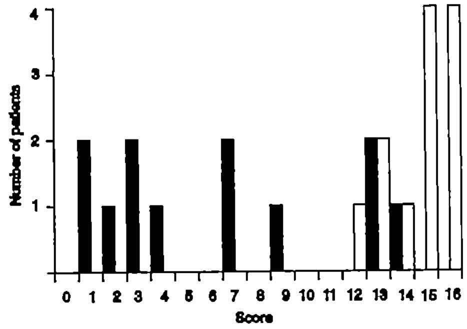

FIG. 3 Distribution of scores on social behaviour item of CBS (maximum score = 16) (■ stuporose, □ non-stuporose).

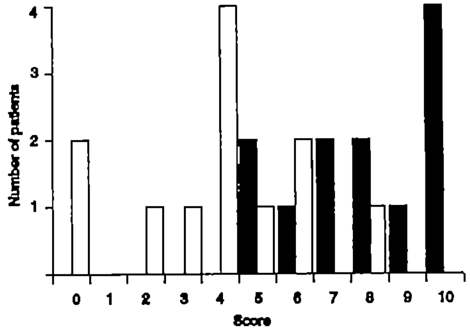

FIG. 4 Distribution of scores on exhibited abnormal behaviour item of CBS (maximum score = 12) (■ stuporose, □ non-stuporose).

Discussion

Although there have been no previous studies of the prognosis of stupor alone with which comparisons may be made, the significance of the catatonic subtype as a whole has been the subject of much debate. Initially, Kraepelin (1919, first published 1913) considered the outlook poor, with Bleuler (1966, first published 1911) in agreement in claiming that catatonic symptoms, when prominent, represented the illness in a severe form. Subsequently, opinions varied widely, with some authors reporting relatively high recovery rates, while others considered deterioration inevitable (Bellinger, 1932), although as time passed the trend became more consistently in favour of a good prognosis for catatonics (Hinsie, 1934; Rupp & Fletcher, 1940), and more recent studies have supported this view (Morrison, 1974*a*; Wortis, 1975). The comtemporary position is of prominent catatonic features auguring well in terms of prognosis (Sainsbury, 1980; Murray, 1986; Goldberg *et al*, 1987).

In our study, despite being in-patients in the same wards in the same hospital for an average of almost 40 years, the initially stuporose patients had fared less well than their fellows. It must not be assumed that the combination of stupor and schizophrenia is necessarily invariably sinister, since the whole sample had a bad prognosis, having stayed in hospital where others unidentified had left; nevertheless, the results may be interpreted as giving some support to the original views of Kraepelin and Bleuler.

An alternative explanation to account for the disparity between the two groups is that the stupor sample did not, and do not, have 'true' schizophrenia at all, but suffer from undiagnosed neurological illness. This notion is not new. That a proportion of 'schizophrenics' presenting in the earlier part of the century, especially those in the catatonic subgroup, had instead organic brain disease has been previously proposed, with encephalitis lethargica appearing as the pre-eminent choice (Mahendra, 1981; Marsden, 1982). This disorder could present in young adults with stupor, other psychoses with schizophrenia-like chronic sequelae being not uncommon (Lishman, 1987), and it is well documented that many cases of encephalitis lethargica were admitted to mental hospitals with 'psychosis', following the great pandemic of 1918–20, before being more correctly diagnosed when post-encephalitic Parkinsonism subsequently ensued (*Lancet*, 1966). It is important to remember in this context, however, that profound motor disturbance following this illness, while common, was by no means inevitable (Lishman, 1987). Furthermore, while the traditional view is that the disease died out in the early 1930s, there is evidence that sporadic outbreaks occurred much later than this (Leigh, 1946; Espir & Spalding, 1956) and indeed continue to be reported (Hunter & Jones, 1966; *Lancet*, 1981). The patients in this study first became ill around the time of World War II. While all presented with typical schizophrenic symptomatology, and certainly fulfilled widely used operational criteria for the disorder, the possibility that the stupor group suffered instead from a lethargica-type encephalitis or similar neurological disorder cannot be dismissed.

References

Abrams, R. & Taylor, M. A. (1976) Catatonia: a prospective clinical study. *Archives of General Psychiatry*, **33**, 579–581.

Achte, K. A. (1961) The course of schizophrenia and schizophreniform psychosis. *Acta Psychiatrica et Neurologica Scandinavica*, **36**, 165; 220–245.

American Psychiatric Association (1980) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn) (DSM–III). Washington, DC: APA.

Bellinger, C. H. (1932) Prognosis in schizophrenia–catatonic form. *Psychiatric Quarterly*, **6**, 475–487.

Berrios, G. E. (1981) Stupor revisited. *Comprehensive Psychiatry*, **22**, 446–478.

Bleuler, E. (1966) *Dementia Praecox, or the Group of Schizophrenias* (trans J. Zinkin). New York: International Universities Press.

Espir, M. L. E. & Spalding, J. M. K. (1956) Three recent cases of encephalitis lethargica. *British Medical Journal*, *i*, 1141–1144.

Fraser, M. (1982) *ECT, A Clinical Guide*. Chichester: Wiley.

Goldberg, D., Benjamin, S. & Creed, F. (1987) *Psychiatry in Medical Practice*. London: Tavistock.

Hinsie, L. E. (1934) The catatonic syndrome in dementia praecox. *Psychiatric Quarterly*, **8**, 457–468.

Hunter, R. & Jones, M. (1966) Acute lethargica type encephalitis. *Lancet*, *ii*, 1023–1024.

Johnson, J. (1982) Stupor: its diagnosis and management. *British Journal of Hospital Medicine*, **27**, 530–532.

Johnstone, E. C., Owens, D. G. C., Frith, C. D., *et al* (1985) Institutionalisation and the outcome of functional psychosis. *British Journal of Psychiatry*, **146**, 36–44.

Joyston-Bechal, H. P. (1966) The clinical features and outcome of stupor. *British Journal of Psychiatry*, **112**, 967–981.

Kraepelin, E. (1919) *Dementia Praecox and Paraphrenia* (trans R. M. Barclay). Edinburgh: Livingstone.

Krawiecka, M., Goldberg, D. & Vaughn, M. (1977) A standardised psychiatric assessment for rating chronic psychotic patients. *Acta Psychiatrica Scandinavica*, **55**, 299–308.

Lancet (1966) Encephalitis of lethargica type in a mental hospital. Leading article. *Lancet*, *ii*, 1014.

—— (1981) Encephalitis lethargica. Leading article. *Lancet*, *ii*, 1396.

Leigh, A. D. (1946) Infections of the nervous system occurring during an epidemic of influenza. *British Medical Journal*, *ii*, 936–938.

Lishman, W. A. (1987) *Organic Psychiatry* (2nd edn). Oxford: Blackwell.

Mahendra, B. (1981) Where have all the catatonics gone? *Psychological Medicine*, **11**, 669–671.

Marsden, C. D. (1982) Motor disorders in schizophrenia. *Psychological Medicine*, **12**, 13–15.

Morrison, J. R. (1974*a*) Catatonia: prediction of outcome. *Comprehensive Psychiatry*, **15**, 317–325.

Morrison, J. R. (1974*b*) Changes in subtype diagnosis of schizophrenia: 1920–1966. *American Journal of Psychiatry*, **131**, 674–677.

Murray, R. (1986) Schizophrenia. In *Essentials of Postgraduate Psychiatry* (eds P. Hill, R. Murray & A. Thorley). London: Grune & Stratton.

Owens, D. G. C. & Johnstone, E. C. (1980) The disabilities of chronic schizophrenia–their nature and the factors contributing to their development. *British Journal of Psychiatry*, **136**, 384–395.

Rupp, C. & Fletcher, E. D. (1940) A five to ten year follow up study of 641 schizophrenic cases. *American Journal of Psychiatry*, **96**, 877–888.

Sainsbury, M. J. (1980) *Key to Psychiatry* (3rd edn). Aylesbury: HM & M.

Wender, P. H. (1963) Dementia praecox, the development of the concept. *American Journal of Psychiatry*, **119**, 1143–1151.

Wortis, J. (1975) Catatonia. *Biological Psychiatry*, **10**, 243.

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Maternity Blues

I. Detection and Measurement by Questionnaire

HELEN KENNERLEY and DENNIS GATH

The studies reported had two purposes: (a) to identify psychological symptoms commonly experienced by mothers in the first few days after childbirth; (b) to use psychometric methods to develop a questionnaire for detecting and measuring these symptoms. A draft 49-item questionnaire was derived by asking 100 newly delivered mothers to volunteer suitable items. The number of items was systematically reduced to 28 while testing the questionnaire on two further samples of newly delivered mothers ($n = 100$ and $n = 50$). Cluster analysis of the 28 items yielded seven clusters, the robustness of which was established in a further sample of 87 newly delivered mothers. The validity of the 28-item questionnaire was established. The questionnaire was quick and easy to administer, suitable for repeated administration on consecutive days, and well accepted by mothers.

'Maternity blues' usually denotes a brief psychological disturbance in mothers in the first few days after childbirth. Maternity blues is generally regarded as a disturbance of mood, but there is little agreement on its precise definition. Weeping and lability of mood are commonly described, but there is disagreement as to whether or not depressed mood is characteristic (Yalom *et al*, 1968; Handley *et al*, 1980; Cox *et al*, 1982). It is usually said that symptoms reach a peak of intensity about four or five days after birth, and then decline fairly rapidly, disappearing before the tenth day. Estimates of the frequency of the blues have ranged widely from 15% of births (Oppenheim, 1962) to 80% (Robin, 1962). More information about research on the blues can be found in reviews by Stein (1982) and by Kennerley & Gath (1986).

Maternity blues is brief and benign, and therefore not a serious problem in clinical practice. Nevertheless, it has interested researchers because it might throw light on the aetiology of mood disorders. So far, most research findings have been inconclusive, possibly because instruments for detecting and measuring the blues have varied in their suitability. For example, standardised psychiatric interviews, such as the Present State Examination (Wing *et al*, 1974) and the Standardised Psychiatric Interview (Goldberg *et al*, 1970), have been used to measure psychiatric symptoms in the early puerperium (George *et al*, 1980; Cox *et al*, 1982). Although well established, these instruments were not designed for measuring the blues, and are not suitable for day-to-day use.

As mood changes may be rapid during the early puerperium, daily assessments are essential. For this purpose a self-evaluation schedule is more practical than daily interviews. Some researchers have studied the blues with self-rating scales originally designed to measure depressive symptoms (Nott *et al*, 1976; Handley *et al*, 1980; Ballinger *et al*, 1982; Manley *et al*, 1982; Cutrona, 1983). Such measures may be better for day-to-day use, but may still be inappropriate because it is not established that depressive symptoms are the main feature of the blues.

Three scales have been designed for measuring the blues (Pitt, 1973; Stein, 1980; Kendell *et al*, 1981), although not developed by systematic psychometric methods. These three scales have between them a total of 28 different items, of which only three are common to all three.

For these reasons, it seemed desirable to devise a further questionnaire to detect and measure maternity blues. The aims of the studies described in this paper were:

(a) to identify psychological symptoms commonly experienced by women in the ten days after childbirth
(b) to use psychometric methods to develop a questionnaire which is suitable for detecting and measuring maternity blues by repeated administration on consecutive days, is short and easy to administer, and is acceptable to mothers
(c) to determine the validity of this questionnaire.

Procedures

Stage 1: compilation of possible items for first draft questionnaire

One hundred newly delivered mothers (group A) were selected for interview in the maternity department of the

TABLE I
Stages of elimination and modification of questionnaire items

Item no.	*Original item (Stage 1)*	*Response frequency (%)*	*Stage 2*		*Stage 3*	
			Redundant	*Infrequent or non-specific*	*Non-peaking*	*Items as they appear in final questionnaire*
1	Tearful	47				Tearful
2	Happy	40				Happy
3	Concentrating poorly	40				Able to concentrate
4	Lively	37				Lively
5	Confident	36				Confident
6	Weeping	33	Similar to 1			
7	Tolerant	33		√		
8	Calm	32				Calm
9	Tired	32				Tired
10	Elated	30				Elated
11	Sleepy	30	Similar to 9			
12	Physically fit	26		√		
13	Alert	24				Alert
14	Oversensitive	24				Oversensitive
15	Restless	23				Restless
16	Overemotional	22				Overemotional
17	Muddled thinking	21	Similar to 21/41			
18	Crying, unable to stop	20				Crying without being able to stop
19	Excited	19	Similar to 10/30			
20	Low spirited	17				Low spirited
21	Forgetful	17				Forgetful, muddled
22	Mentally relaxed	16				Mentally relaxed
23	Physically relaxed	16		√		
24	Emotionally reserved	13				Finding it difficult to show my feelings
25	Relieved	11		√		
26	Brooding	11				Brooding on things
27	Optimistic	11		√		
28	Purposeful	11			√	
29	Emotionally stable	11				Up and down in mood
30	Content	10	Similar to 10/19			
31	Over-reacting	10	Similar to 14			Changeable in mood
32	Changeable in mood	9				
33	Bonding poorly	9			√	
34	Mentally tense	7				Mentally tense
35	Lacking interest	6			√	
36	Care-free	5	Similar to 22			
37	Irritable	5				Irritable
38	Hostile, touchy	5	Similar to 37			
39	Emotionally numb	4				Emotionally numb, without feelings
40	Physically tense	4		√		
41	Slow in thinking	3	Similar to 17/21			
42	Self-pitying	2				Feeling sorry for myself
43	Helpless	2				Helpless
44	Socially withdrawn	2				Wishing that I was alone
45	Depressed	2				Depressed
46	Disorientated	2		√		
47	Anxious	1				Anxious
48	Earnest	1		√		
49	Possessive	1			√	

local teaching hospital. Each mother was interviewed once in the ten days immediately after childbirth: 74 interviews were held on days 1–6; and 26 on days 7–10, most mothers having left hospital by then. This difference was not thought important because the purpose was simply to compile suitable adjectives for the first draft questionnaire.

Interviewing was unstructured. Mothers were simply asked to describe in their own words the feelings they had experienced at any time that day, and to indicate whether these feelings differed in any way from their normal feelings (before pregnancy). Most mothers had no difficulty in putting their feelings into words. The interviewer helped the few who had difficulty by suggesting some common mood adjectives to start them talking. Interviews lasted about 30 minutes and all were tape-recorded.

Analysis of items

Of the 100 women interviewed in group A, 47 reported unusual feelings on the day in question; all 47 were interviewed on one of the first five days. Of the 53 women reporting no such experiences, 21 were interviewed in the first five days, and 32 on days 6–10.

The tape-recordings were used to compile a list of adjectives used by the 47 women, and to determine their frequency (Table I). It is notable that the term 'depressed' was used by only 2% of respondents, while 'low spirited' was used by 17%.

'Confusion' has often been cited as a feature of maternity blues. In the present sample, 'concentrating poorly' and 'muddled thinking' were commonly reported. However, there was no evidence that these symptoms were associated with organic mental states, since item 46, 'disorientated', was reported by only 2% of the mothers, and at interview there was no clinical evidence of either disorientation or clouding of consciousness in any respondent.

Stage 2: administration and revision of first draft questionnaire

The 49 items elicited in stage 1 were assembled in random order in a draft questionnaire. Each item was rated on the following five-point scale: much less than usual; less than usual; same as usual; more than usual; much more than usual.

The questionnaire was administered to a second group of 100 mothers (group B) who were in the maternity ward for up to ten days after childbirth. It was then shortened by eliminating items which, as shown in Table I, were:

(a) redundant, that is, highly correlating items which appeared to be measuring the same psychological dimension (items 6, 11, 17, 19, 30, 31, 36, 38, 41)
(b) infrequently endorsed, that is, rated by less than 15% of mothers (items 7, 46, 48)
(c) non-specific (items 25, 27) or descriptive of physical states (items 12, 23, 40).

Stage 3: administration and revision of second draft questionnaire

The second draft questionnaire (as revised in stage 2) was given to a further 50 mothers (group C) who were in hospital up to ten days after childbirth. Each mother was asked to complete the questionnaire on the day it was given to her and again on the following day. Ratings were to be made in the evening, and were to apply to the day as a whole.

At this stage four items were removed, as they failed to show a peak of frequency in the first few days (Table I, items 28, 33, 35, 49). These were omitted because past research findings and clinical observations had suggested that peaking is characteristic of the blues. In this way the number of items was reduced to its final total of 28. The final version of the questionnaire is shown in the Appendix.

Stage 4: cluster analysis and scoring system

Cluster analysis and labelling of clusters

The next step was to determine whether the 28-item questionnaire was measuring one or more different syndromes. For this purpose, the statistical technique of cluster analysis was preferred to other forms of factor analysis because it has been specifically designed as a means of sorting sample data in terms of typography. This technique is especially appropriate when little is known about category structure within the data. The purpose of the technique is to sort data into clusters such that the degree of association is high among members of the same cluster, and low among members of different clusters (Everitt, 1974). In our analysis, mothers' responses were subjected to Ward's method of clustering, using the computer program CLUSTAN (Wishart, 1975).

The clusters comprised items, not subjects, and the similarity measure used was based on the squared Euclidean distances between items. Analysis using Ward's method of clustering produced a dendogram of clusters. The cut-off point used to determine the most meaningful grouping of items is arbitrary, but it is generally taken to be the first large increase in increment in the error coefficient (the latter being the sum of distances from each individual item to the centroid of its parent cluster).

To ensure that the scale would measure change from normal state, and that clusters would be homogeneous, responses were entered into the cluster analysis only when the respondent rated seven or more of the 28 items as applying to her on the day in question. Of the 100 sets of responses (50 group C subjects × 2 days), the number meeting this criterion was 32. Seven clusters emerged (Table II). From inspection of the components of clusters, and bearing in mind the direction of rating (see 'scoring system', below), the investigators gave a label to each cluster, as shown in Table II.

Scoring system

When the daily frequencies of the 28 items were plotted graphically (not shown) it was found that 20 items showed a peak when rated 'more than usual', and eight items when rated 'less than usual' (Table II).

It was decided to allocate a score of 1 to each of the 20 items showing a peak when rated 'more than usual' or 'much more than usual', and to each of the eight items showing a peak when rated 'less than usual', or 'much less

TABLE II
Composition and labelling of clusters

Cluster label	*Component items*	
	Group C (n=32)	*Group D (n=87)*
1. Primary blues	Tearful	Tearful
	Tired	—
	Anxious	—
	Overemotional	Overemotional
	Changeable in mood	Changeable in mood
	Low spirited	Low spirited
	Forgetful/muddled	—
		Up and down in mood
		Oversensitive
2. Reservation	Emotionally reserved	Emotionally reserved
	Emotionally numb without feeling	Emotionally numb without feeling
	Socially withdrawn	Socially withdrawn
3. Hypersensitivity	Mentally tense	
	Restless	
	Oversensitive	
	Up and down in mood	
4. Depression	Brooding on things	Brooding on things
	Irritable	Irritable
	Depressed	Depressed
	Self-pitying	Self-pitying
	Crying without being able to stop	—
		Confident[1]
		Mentally tense
		Anxious
		Restless
5. Despondency	Elated[1]	Elated[1]
	Helpless	—
	Happy[1]	Happy[1]
6. Retardation	Able to concentrate[1]	Able to concentrate[1]
	Alert[1]	Alert[1]
	Lively[1]	Mentally relaxed[1]
		Calm[1]
7. Decreased self-confidence	Confident[1]	
	Mentally relaxed[1]	
	Calm[1]	
New cluster 1		Tired[1]
		Lively
New cluster 2		Helpless
		Forgetful/muddled
		Crying without being able to stop

1. Items rated in direction 'less than usual' (all other items rated 'more than usual').

than usual'. In this way, each respondent could be given an overall score (maximum 28) and a subscore for each cluster (the maximum varying according to the number of items in the cluster), thereby indicating the nature and the severity of her condition.

Thus we used the data categorically (absent = 0; present = 1) and did not attempt to measure severity by using the data dimensionally. This was because a range of responses might not indicate severity but rather individual scoring style (i.e. tendency to be conservative or extreme). In paper III we describe how this system can be employed in the analysis of continuous and discrete variables.

If preferred, the five-point scale (see Appendix) could be used to assess severity of an item by scoring 'more (less) than usual' as 1 and 'much more (less) than usual' as 2. We suggest that the number of options should not be increased to more than these five as it has been established that more complex scoring methods confer no real advantage (Likert, 1932).

Cluster frequency

By using the categorical scoring system, it was possible to determine the frequency of each cluster among the 50 women in group C. This was done for each cluster by determining how many women scored on more than half the items in the cluster. On this basis the proportions of respondents were: primary blues 36%; retardation 36%; hypersensitivity 26%; decreased self-confidence 24%; depression 16%; reservation 10%; despondency 8%.

Stage 5: administration of final 28-item questionnaire

Testing the robustness of clusters

The final 28-item questionnaire was completed by a further sample of 87 newly delivered women (group D) every day during the first ten days after childbirth.

By comparing group C and group D, the robustness of clusters was shown in two ways. (a) When the responses of group D were subdivided according to the clusters originally derived from group C responses, the frequency of the seven clusters followed almost the same rank order in both groups. (b) When a new cluster analysis was carried out on group D responses, the new clusters were similar in composition to the original group C clusters. This degree of resemblance is unusually close considering that cluster analysis was applied to a different group at a different time.

Day-to-day variation in responses

Figure 1 shows the mean percentage scores on the questionnaire for group D women on each of the ten post-natal days. Mean percentage scores were derived as follows. For each individual woman, a total score for each of the ten days was expressed as a percentage of the items completed by her (this was done to allow for occasional missing values). A mean percentage score for each of the ten days was then derived for the sample as a whole, together with an overall mean value for the ten days as a whole. It can be seen that the scores reached a peak (24.3%) on day 5, and tailed off towards day 10. Analysis of variance, however, showed that the pattern of distribution of the scores did not differ significantly from chance. (However, a subsequent study using this questionnaire has shown statistically significant peaking of scores – see 'Discussion'.)

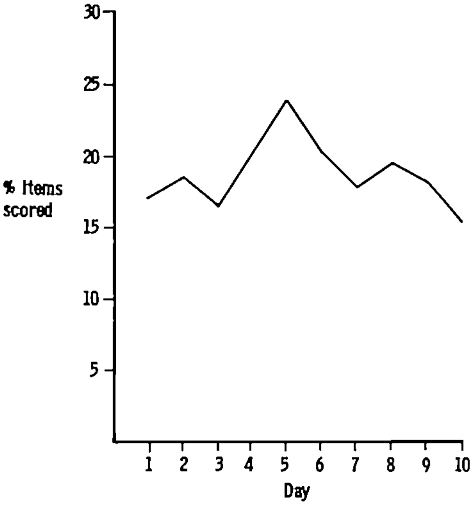


FIG. 1 Mean scores on the questionnaire during the first ten days after childbirth. For each woman, a total score for each of the ten days was expressed as a percentage of the items completed by her (to allow for occasional missing values). A mean percentage score for each of the ten days was then derived for the sample as a whole.

Figure 2 shows the percentage item scores for individual clusters for group D women on each of the ten post-natal days. It can be seen that the clusters appear to co-vary, and most clusters tend to peak in frequency about the fifth day.

Validity of the questionnaire

The questionnaire was devised to detect symptoms which might change rapidly. For this reason the reliability of the questionnaire could not be tested by administering it to the same woman on separate occasions. However, when the questionnaire was given first to group C and then to the similar but completely independent sample, group D, response patterns were found to be stable in two ways: first, symptoms tended to peak on the same post-partum day in both groups; second, as explained above, patterns of clustering were very similar in the two groups.

Content validity was supported in three ways: the use of open-ended inquiry to elicit an original pool of items from 100 mothers (group A) is one of the most powerful demonstrations of content validity possible; the samples of mothers were highly representative because over 95% of mothers from the catchment area are delivered in the hospital concerned; and four different samples of mothers were used.

Face validity was supported by the fact that subsequent groups of mothers found the questionnaire items acceptable and appropriate.

Construct validity was shown in the following four ways.

(a) 'Primary blues' emerged as a distinct cluster from 'depression' and was much more frequent. This was true for mothers in both groups C and D.

(b) Of the 87 mothers in group D, 79 completed the questionnaire not only post-natally but also over a three-day period four weeks antenatally. Scores were significantly higher post-natally. Thus the mean total percentage of items endorsed increased from 14.8% antenatally to 21.3% post-natally ($t=2.85$; d.f. 78; $P<0.001$), while the mean peak score increased from 23.6 to 45.7 ($t=6.06$; d.f. 78; $P<0.001$). It is important to note that cluster scores changed significantly in only two clusters. Thus the score for 'primary blues' increased from 19.6 antenatally to 27.8 post-natally ($t=3.78$; d.f. $=11$; $P<0.01$), and for 'hypersensitivity' from 17.6 antenatally to 22.6 post-natally ($t=3.45$; d.f. $=1$; $P<0.01$). Scores for the remaining clusters (which contained some items traditionally ascribed to 'maternity blues') did not change. These findings supported the argument that changes in depression are not characteristic of the early puerperium.

(c) All clusters except despondency showed a tendency to peak about day 5 (in line with symptom peaking as reported by other investigators).

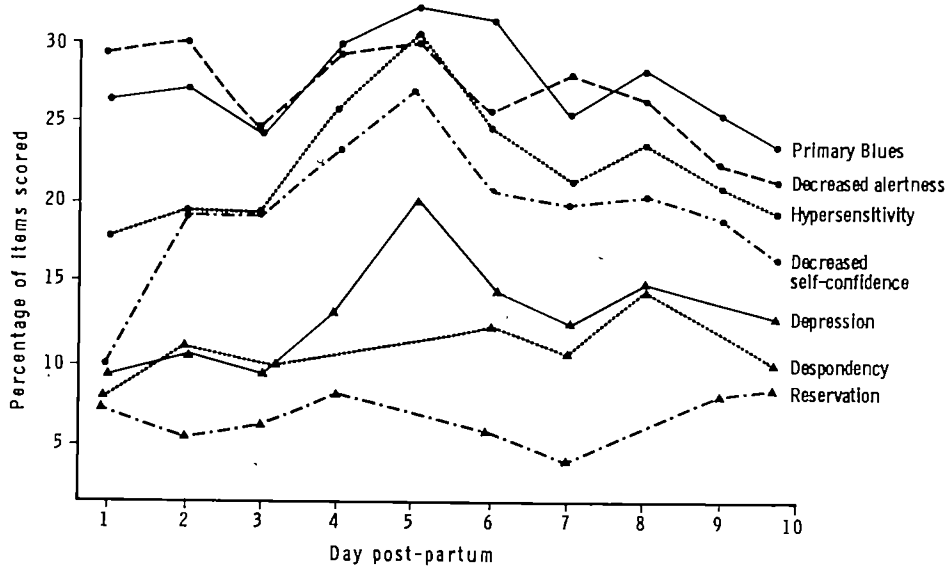


FIG. 2 Cluster scores on the questionnaire during the first ten days after childbirth.

(d) In a separate study (paper II) it was found that whereas questionnaire scores tended to peak on the fourth or fifth post-natal day in maternity patients, in surgical patients they tended to peak on the second post-operative day and then declined steadily.

Discussion

Asking subjects to volunteer words describing their feelings gives the advantage that items elicited are both relevant and acceptable to the population studied (Mackay, 1980). By eliminating redundant items by systematic item analysis, the final questionnaire was reduced to 28 items which could be grouped into seven clusters. Studying a further sample confirmed the validity of the questionnaire and established the robustness of clusters.

Our questionnaire differs in several ways from the three best-known measures designed to rate the blues. Among the latter, the rating scale devised by Pitt (1973) was based on Hamilton's (1962) account of the blues, which listed eight symptoms that midwives regarded as most frequent in the mid-puerperium: fatigue, crying, anxiety, confusion, headache, insomnia, hypochondriasis, and hostility to husband. Pitt added 'depression' to this list. In our questionnaire, there are only four items that appear to correspond to these nine items (tired, tearful, anxious, and, possibly, muddled thinking).

The questionnaire devised by Stein (1980) contained 13 items (depression, weeping, restlessness, anxiety, fatigue, tension, irritability, poor concentration, forgetfulness, confusion, anorexia, dreaming, and headache). The first nine of these items correspond approximately to items in our questionnaire. Another of Stein's items, 'confusion', may correspond to our 'forgetful/muddled'. Three of Stein's items (anorexia, dreaming, and headaches) have no counterpart in our questionnaire, and 18 of our items do not appear in Stein's questionnaire. It is notable that all these differences between the two questionnaires were present in stage 1 of the development of our questionnaire. In other words the differences may have occurred because our first procedure was based on eliciting adjectives directly from the mothers.

Our questionnaire contained corresponding items for all six items which Kendell *et al* (1981) included in their six visual analogue scales, namely happiness, depression, tears, anxiety, irritability, and lability.

Two points about our questionnaire are stressed. First, when the questionnaire was administered over a ten-day period, mean scores appeared to peak on day 5, but day-to-day variation was not statistically significant. Subsequently, however, Owen & Campbell (1987) gave the questionnaire to a further sample of women and found a statistically significant peaking of scores on the third day post-partum.

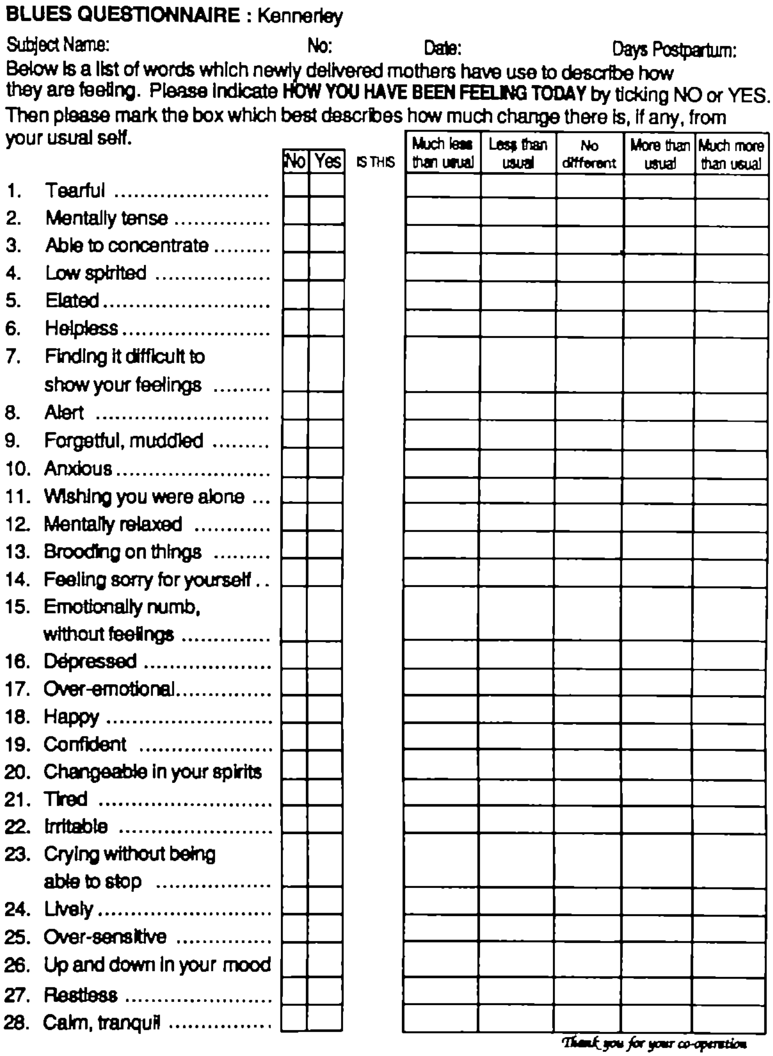
Second, the clusters threw some light on the question of whether depression is characteristic of maternity blues. The most frequent cluster, which we called 'primary blues', included the item 'low spirited', whereas a less frequent cluster, 'depression', included the item 'depressed'. A possible explanation is that the mothers used 'low spirited' to denote a demoralised state of low intensity, and 'depressed' to indicate a more severe dysphoria. Mothers frequently stated, "I don't feel depressed but I do feel low spirited". Thus the findings suggested that depression is not typical of the blues.

Conclusions

Our questionnaire is valid for detecting and measuring specific brief psychological disturbances occurring in the first few days after childbirth. The questionnaire should be suitable for future research on the aetiology of maternity blues (whether psychological or biological) and on the associations between the blues and previous or subsequent psychiatric disorder.

Appendix

The questionnaire is reproduced below. It was modified to include the columns headed 'no' and 'yes' because women said that it would be easier to answer the questionnaire in two steps – deciding first whether the item applied to them at all, and then (if it did apply) deciding to what extent. This change made the instrument more acceptable to mothers without altering the psychometric properties of the data collected.



BLUES QUESTIONNAIRE : Kennerley

Subject Name: No: Date: Days Postpartum:

Below is a list of words which newly delivered mothers have use to describe how they are feeling. Please indicate **HOW YOU HAVE BEEN FEELING TODAY** by ticking NO or YES. Then please mark the box which best describes how much change there is, if any, from your usual self.

	No	Yes	IS THIS	Much less than usual	Less than usual	No different	More than usual	Much more than usual
1. Tearful								
2. Mentally tense								
3. Able to concentrate								
4. Low spirited								
5. Elated								
6. Helpless								
7. Finding it difficult to show your feelings								
8. Alert								
9. Forgetful, muddled								
10. Anxious								
11. Wishing you were alone								
12. Mentally relaxed								
13. Brooding on things								
14. Feeling sorry for yourself								
15. Emotionally numb, without feelings								
16. Depressed								
17. Over-emotional								
18. Happy								
19. Confident								
20. Changeable in your spirits								
21. Tired								
22. Irritable								
23. Crying without being able to stop								
24. Lively								
25. Over-sensitive								
26. Up and down in your mood								
27. Restless								
28. Calm, tranquil								

Thank you for your co-operation

References and authors' details will be found at the end of paper III, on page 373.

British Journal of Psychiatry (1989), **155**, 363–366

Maternity Blues

II. A Comparison Between Post-operative Women and Post-natal Women

SUSAN ILES, DENNIS GATH and HELEN KENNERLEY

A new scale for the detection and assessment of maternity blues was completed by 56 women daily for ten days after elective gynaecological surgery. When their responses were compared with those of 87 post-natal women, they differed significantly in frequencies of different symptoms at different times. The findings suggest that post-natal mood changes ('maternity blues') are characteristic of the puerperium and not simply non-specific reactions to physical and emotional stress.

There are two different views of 'maternity blues'. One is that the symptoms are characteristic in timing and intensity, and differ in these ways from symptoms after other types of stressful event. Related to this view is the suggestion that maternity blues may be induced by particular endocrine changes in the early puerperium. The other view is that maternity blues is not specific to childbirth but is a general 'end reaction' that can occur after any physical stressor (Yalom *et al*, 1968).

The main aim of the present study was to examine these two conflicting views by comparing the responses of post-operative and post-natal women on a new maternity blues scale (paper I). A further aim in studying the post-operative group was to compare their pre-operative psychological status with their post-operative blues scores.

Method

Recruitment of patients

Post-operative patients

These women were recruited over a four-month period from all women aged 18–40 who were admitted (on designated research days) to hospital in Oxford, for elective gynaecological surgery. The age range corresponded with that of the post-natal group (see below). The patients were recruited on the day before surgery, which was nearly always the day of admission.

Sixty-eight women entered the study, of whom 12 were excluded later because they did not provide complete daily ratings for ten post-operative days (the reason usually being that they felt too unwell at the time). The remaining 56 women provided complete recordings, and were included in the study. They were having a variety of surgical procedures (see 'Results').

Gynaecological surgery was chosen because it would not be associated with the endocrine changes characteristic of childbirth, but would probably present the patients with some similar psychological stressors.

Post-natal patients

These were 87 recently delivered women who returned full sets of questionnaires completed daily for ten days after childbirth (see paper I, group D).

Pre-operative interview

On the day before surgery, the post-operative patients were given an explanation of the study, and were asked to complete a questionnaire daily on the first ten post-operative days. They were not told that the questionnaire was designed for use in the puerperium. One investigator (SI) then interviewed each patient, using a semistructured schedule, to obtain obstetric, medical, and psychiatric histories, together with social and demographic information.

Although the study was mainly concerned with post-operative scores on the maternity blues scale, the opportunity was taken to administer the following scales before the operation: General Health Questionnaire (GHQ; Goldberg, 1972); Leeds Scales for Anxiety and Depression (Snaith *et al*, 1976); Modified Social Adjustment Scale (SAS-M; Cooper *et al*, 1982); Eysenck Personality Inventory (Eysenck & Eysenck, 1964).

Post-operative assessments

Each patient awaiting gynaecological surgery was given ten copies of the new blues questionnaire and was asked to complete it at the same time on each of ten consecutive evenings, starting on the first day after the operation.

One investigator (SI) visited the patients regularly in hospital to deal with any problems in completing the questionnaire. If patients were discharged before the tenth post-operative day, they were asked to continue completing their forms at home and to return them by post. Such patients were telephoned at home to deal with any problems in completing the questionnaire. Reminders were sent to any women who did not return their questionnaires within 14 days after the tenth post-operative day.

Data analysis

The blues scores

Responses of the 56 post-operative women were analysed in the same way as previously for the 87 post-natal women. Three main methods were used. First, total scores were calculated for each woman for each of the ten post-operative days. A mean percentage score for each of the ten days was then derived for the sample as a whole, together with an overall mean value for the ten days as a whole (see paper I, p. 356). Second, questionnaire responses were examined by cluster analysis, using the computer program CLUSTAN (Wishart, 1975). Third, analysis of variance was used to assess the significance of differences in scores between each of the ten post-operative days. Analysis of variance was also used to compare results from the surgical women with those from the post-natal women.

Relationship between blues scores and pre-operative measures

For each woman in the post-operative group, the relationship between her mean blues score over the ten post-operative days and her scores on pre-operative measures was examined with t-tests for discontinuous variables (for example, type of operation) and with Pearson's test for continuous variables (for example, GHQ total scores).

Results

Patient characteristics

Women in the post-operative and post-natal groups did not differ significantly in age, marital status, or psychiatric history.

The 56 post-operative patients fell into two main groups: 33 who had major, and 23 who had minor surgery. The former consisted of 25 women who had a hysterectomy (four of them for carcinoma of the cervix), and eight who had other procedures involving laparotomy (e.g. ovarian cystectomy, division of pelvic adhesions, tubal reconstruction). The group undergoing minor surgery consisted of 17 women who had procedures such as dilatation and curettage, laparoscopy, cystoscopy, and examination under anaesthesia (often in combination), together with six who had a cone biopsy for carcinoma of the cervix.

Scores on the blues questionnaire

In Fig. 1, daily mean percentage scores are given for both groups of women. It can be seen from Fig. 1 that scores were higher among the post-operative women than among the post-natal women throughout the ten-day period. The overall mean percentage scores for the ten days as a whole were 31.5 (s.d. 7.77) for post-operative women, and 18.5 (s.d. 2.49) for post-natal women.

In the post-operative group mean percentage scores declined steadily from 42.9% on day 2 to 21.7% on day 10. Analysis of variance showed that the distribution of the daily scores over ten days differed significantly from chance ($F=7.91$, d.f. $=9$, $P<0.001$). In the post-natal group, mean percentage scores reached a peak (24.3%) on day 5, and tailed off towards day 10. When the mean percentage scores of the two groups of women were compared by analysis of variance, significant differences were found between their patterns of distribution over ten days ($F=4.22$, d.f. $=9$, $P<0.001$).

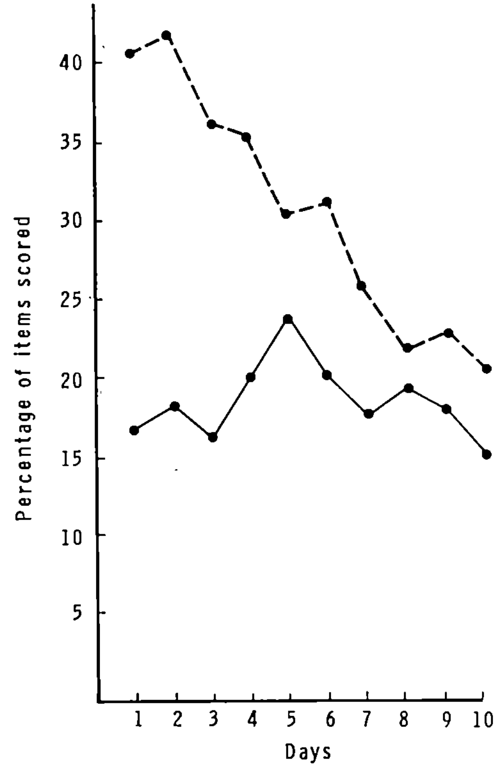


FIG. 1 Day-by-day distribution of total blues scores: comparison of post-partum (————) and post-operative (----) women.

Cluster analysis

When the responses of post-operative women were examined by cluster analysis, the resulting clusters were similar to those previously found in the 87 post-natal women (group D) and also in a separate group of 32 post-natal women (group C) (see paper I, Table II), although there were some minor discrepancies. (The matching of clusters in these three groups (one post-operative and two post-natal) is too detailed for presentation here but can be supplied on application.)

The resemblance of clusters made it possible to compare the patterns of scoring of post-operative and post-natal women. For each of the ten days, cluster frequency was determined by calculating the numbers of women scoring on more than half the items in a cluster; these numbers were then expressed as percentages of the numbers of women completing the questionnaire. Among post-operative women, the most frequently endorsed cluster was 'retardation', followed by 'decreased self-confidence'. Among post-natal women, however, the most frequently endorsed cluster was 'primary blues', followed by 'retardation' and 'hypersensitivity'. In both groups, the least frequent clusters were 'depression', 'despondency' and 'reservation'. Cluster scoring over the ten-day period is shown graphically for post-operative women in Fig. 2. It can be seen that the clusters appear to co-vary, with a tendency to decline over the ten-day period. By contrast, among post-natal women it had previously been found that most clusters tended to peak in frequency about the fifth day (see paper I).

Pre-operative assessment

Mood scales

GHQ On the day before surgery, 32 of the 56 surgical women were potential cases as determined by a score of 12 or over on the 60-item GHQ. Total GHQ scores did not differ significantly between women having major operations (mean 13.85, s.d. 12.48) and those having minor operations (mean 17.87, s.d. 13.95) (*t*-test: $t=1.13$, d.f.$=54$, $P=0.263$).

Leeds scales for anxiety and depression On the Leeds scales completed on the day before surgery, 34 of the 56 surgical women scored at or above the cut-off of 7 for anxiety, whereas only 14 (25%) scored 7 or more for depression. Scores for anxiety and depression did not differ significantly between women having major surgery (for anxiety, mean 7.70, s.d. 3.89; for depression, mean 4.94, s.d. 2.46) and those having minor surgery (for anxiety, mean 7.91, s.d. 3.84; for depression, mean 5.65, s.d. 3.68) (*t*-test: $t=0.21$, d.f.$=54$, $P=0.838$ for anxiety; $t=0.87$, d.f.$=54$, $P=0.424$ for depression).

Relationship between blues scores and pre-operative measures

Psychological factors. Among the post-operative patients the following pre-operative measures were significantly associated with post-operative blues mean scores: GHQ total score (Pearson's $r=0.55$, $P<0.001$); Leeds anxiety score (Pearson's $r=0.55$, $P<0.001$); Leeds depression score (Pearson's $r=0.48$, $P<0.001$); and EPI neuroticism (Pearson's $r=0.50$, $P<0.001$). Mean blues scores of women who were GHQ potential cases on the day before surgery ('Bluemean' (see paper III, p. 367) 38.07, s.d. 17.16) were significantly higher than those of women who were not potential cases ('Bluemean' 23.70, s.d. 16.21) (*t*-test: $t=3.13$, $P<0.01$, d.f.$=52$). On Pearson's test there was a significant association between mean blues scores and a history of past episodes of psychiatric consultation with a general practitioner ($r=0.34$, $P<0.01$).

Social functioning. Poor overall social adjustment, as assessed by the SAS-M, was significantly associated with mean blues scores (Pearson's $r=0.33$, $P<0.05$).

Physical health. There were no significant associations between mean blues scores and the subjects' physical health

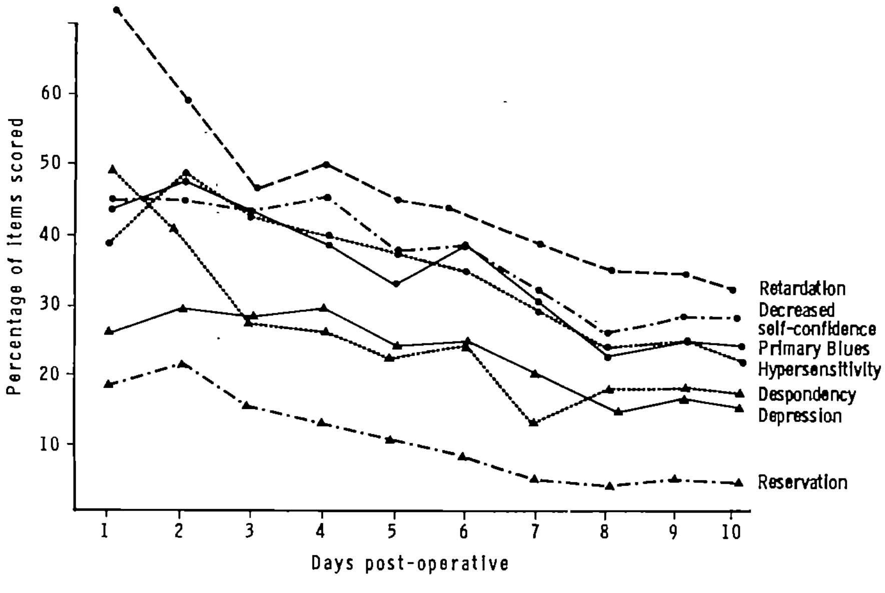


FIG. 2 Day-by-day distribution of cluster scores in post-operative women.

in the past year as evaluated by consultations with general practitioners or by hospital visits.

Blues scores versus type of surgery

Mean blues scores of women undergoing major surgery ('Bluemean' 33.27, s.d. 18.27) did not differ significantly from those of women undergoing minor surgery ('Bluemean' 29.18, s.d. 17.94) (*t*-test: $t=0.8$, $P=0.42$, d.f. $=52$).

Discussion

Scores on the new maternity blues questionnaire differed significantly between post-operative and post-natal women in the ten days after surgery/childbirth: post-operative women had significantly higher scores throughout the ten days and their scores declined steadily from the second to the tenth post-operative day, while those of post-natal women peaked about the fourth or fifth day. When the data were examined by cluster analysis, cluster scores also declined steadily over the ten days in post-operative women, while peaking about day 5 in post-natal women.

These findings closely resemble those of Kendell *et al* (1984), who used a six-item visual analogue scale to compare mood in post-hysterectomy and post-natal women in Edinburgh. The findings here and from Edinburgh indicate that maternity blues is a distinct condition and not just a non-specific 'end reaction' to stressors. However, a different conclusion was drawn by Levy (1986), who used the blues questionnaire of Stein (1980) to compare post-operative and post-natal women. The results generally resembled those found here and in Edinburgh, but among post-operative women some individual items did peak. From this Levy concluded that "the dysphoria called Maternity Blues is not unique to the puerperium".

The findings here and in Edinburgh were strikingly similar. How are these findings to be explained? The explanation may be physical, psychological, or both.

Among physical factors, hormones may be important. For example, mood may be influenced by changes in cortisol in post-operative women, and by changes in oestrogen and progesterone in post-natal women. Despite careful research, no such association between mood and hormones has been confirmed.

Another physical explanation may be that anaesthesia influences mood in post-operative women. This could explain two findings among the 56 post-operative women here: that their mean blues scores were high in the first and second post-operative days, and then declined; and that their most frequent symptom cluster was 'retardation' (consisting of reduced concentration, reduced alertness, and reduced liveliness).

A third physical factor could be the degree of physical trauma. However, post-operative responses to the blues questionnaire did not differ significantly between major and minor surgery, and the responses of post-natal women were not related to complicated labour or physical problems in the puerperium (see paper III).

Among psychological factors, neuroticism may be important. In Oxford and Edinburgh 'neuroticism' scores on the EPI (measured before surgery/delivery) were significantly associated with post-operative/post-natal scores on the blues scales. This finding is consistent with many reports that emotional responses to life events are more severe in neurotic people; and also with the finding that pre-operative neuroticism is significantly associated with complicated or delayed recovery after surgery (Matheus & Ridgeway, 1981).

Another psychological explanation could be that levels of anxiety differ before surgery and childbirth. It has been reported that high pre-operative anxiety is followed by high anxiety after surgery (Johnston, 1980). Among our surgical patients, on the day before surgery 51% scored high on the GHQ and 61% on the Leeds Anxiety Scale. There are no comparable data for the childbirth group, in whom anxiety was measured much earlier in pregnancy. However, it is understandable that surgery is likely to be anticipated with anxiety about the nature of any disease and the outcome, whereas childbirth is generally anticipated as a happy event.

Both the physical and the psychological factors mentioned above could explain the greater severity of blues scores among post-operative women, but it is difficult to see how they could explain the peaking of scores in post-natal women.

We conclude that in post-natal women maternity blues is a distinct puerperal condition, not just a non-specific 'end reaction' to stressful experience. It is less severe than the emotional distress that follows gynaecological surgery. The most distinctive feature of maternity blues is peaking about the third or fourth post-natal day; the cause of this peaking is yet to be found.

References and authors' details will be found at the end of paper III, page 373.

British Journal of Psychiatry (1989), **155**, 367–373

Maternity Blues

III. Associations with Obstetric, Psychological, and Psychiatric Factors

HELEN KENNERLEY and DENNIS GATH

One hundred and six women were assessed psychiatrically in the 14–16th and 36–38th weeks of pregnancy and the 12th week after childbirth. They also completed a maternity blues questionnaire daily in the ten days after delivery. Blues scores were significantly associated with: neuroticism; anxiety and depressed mood during pregnancy; fear of labour; poor social adjustment; and retrospective severity of pre-menstrual tension. Blues scores were not associated with obstetric factors, with previous history of psychiatric disorder, or with case status on the PSE in pregnancy or 12 weeks after delivery.

In the two preceding papers, an account was given of the development and evaluation of a questionnaire for detecting and measuring maternity blues. This paper reports a study in which this questionnaire was used to examine the frequency and severity of the blues in relation to social, obstetric, psychological, and psychiatric factors.

There have been few reports of positive associations between the blues and social factors. The blues has been found to be associated with marital disharmony and with psychosexual problems (Nillson, 1972; Ballinger *et al*, 1979; Cutrona, 1983), but not with social class (Jarrahi-Zadah *et al*, 1969; Stein, 1980) and not with life events or chronic background difficulties (Davidson, 1972; Pitt, 1973; Ballinger *et al*, 1979; Paykel *et al*, 1980; Stein, 1980).

The evidence for associations between the blues and obstetric factors is conflicting. The blues has been reported to be more common in primiparous women (Yalom *et al*, 1968; Nott *et al*, 1976), more common in multiparous women (Davidson, 1972), and not related to parity at all (Robin, 1962; Pitt, 1973; Handley *et al*, 1980; Stein, 1980). Obstetric problems in pregnancy have been found to be associated with the blues by some workers (Yalom *et al*, 1968; Davidson, 1972), but not by others (Pitt, 1973; Ballinger *et al*, 1979; Stein, 1980). It has been suggested that intensive physiological monitoring in labour may be associated with the blues (Oakley & Chamberlain, 1982), but a study by Long Blumberg (1980) did not support such a link. In another study, neither Caesarean section nor length of confinement was found to be associated with the blues (Kendell *et al*, 1984). There seems to be agreement that the frequency of the blues is no different between breast-feeding and bottle-feeding mothers (Ballinger *et al*, 1979; Harris, 1980; Kendell *et al*, 1981; Cox *et al*, 1982). Feeding difficulties and the blues were found to be associated by Pitt (1973), but not by other workers (Harris, 1980; Kendell *et al*, 1981; Cox *et al*, 1982).

Psychological evidence is also conflicting. In studies by Pitt (1973) and by Nott *et al* (1976), no significant associations were found between the blues and scores on the Eysenck Personality Inventory (EPI; Eysenck & Eysenck, 1964). In another study, however, the peaking of blues symptoms on the third and fourth days after delivery was greater in women with higher EPI neuroticism scores (Kendell *et al*, 1984). There has been similar disparity in reports about patients' attitudes. Thus the blues was found to be associated with rejecting or ambivalent attitudes to pregnancy (Nillson & Almgren, 1970), and with fear of labour (Yalom *et al*, 1968), but other workers found no such relationships (Pitt, 1973; Ballinger *et al*, 1979).

The main psychiatric interest has been in possible associations between the blues and affective disorders. The evidence about previous affective disorders is difficult to evaluate, because most studies have examined previous psychiatric disorders in general, rather than affective disorders in particular. The blues has been reported to be associated with previous non-puerperal disorders, including depression (Ballinger *et al*, 1979; Stein, 1980) and mental illness in general (Nillson & Almgren, 1970), but most investigators have found no such relationships (Yalom *et al*, 1968; Pitt, 1973; Handley *et al*, 1980; Harris, 1980; Stein, 1980). The blues has also been found related to previous puerperal depression (Yalom *et al*, 1968; Harris, 1980; Stein 1980).

There is more agreement about the blues in relation to psychiatric symptoms in the index pregnancy. In five studies, associations were found between the blues and symptoms such as anxiety, depression, and weeping in pregnancy (Davidson, 1972; Nott *et al*, 1976; Handley *et al*, 1980; Harris, 1980; Stein, 1980).

The evidence for an association between the blues and subsequent affective disorder is also difficult to evaluate because most studies have been retrospective, and such retrospective recall is likely to be inaccurate. In a prospective study, Cox *et al* (1982) found that women with severe maternity blues (measured on a visual analogue scale) had a higher risk of later persistent depressive symptoms.

There have been two other limitations in previous research: first, the blues was mainly measured with scales that were not designed for the purpose; second, the risk of affective disorder was examined in relation to the occurrence, but not the severity, of the blues.

For these reasons, it was decided to undertake a prospective study in which the blues would be measured daily during the ten days after delivery, and psychiatric state would be measured twice in the index pregnancy, and again in the 12th week after delivery. The aim was to examine both the frequency and severity of the blues in relation to social, obstetric, psychological and psychiatric factors.

Method

Selection of patients

The study was based on a consecutive series of pregnant women who were booked to have their baby in the local maternity unit. A total of 122 women were approached in the 12–14th week of pregnancy and asked to join the study, of whom 112 (92%) agreed to do so.

Assessment procedures

Assessments were made at four stages: (a) weeks 14–16 of pregnancy; (b) weeks 36–38 of pregnancy; (c) the first ten days after the day of delivery; (d) week 12 of the puerperium. In assessment (a) (weeks 14–16 of pregnancy), psychiatric state was rated at interview by means of the Present State Examination (PSE; Wing *et al*, 1974), and symptoms of depression were rated with the scale of Montgomery & Åsberg (1979). Life events were recorded with the interview for recent life events (Paykel *et al*, 1980).

The following self-rated scales were used: Leeds scales for measuring anxiety and depressed mood (Snaith *et al*, 1976); the Modified Social Adjustment Scale (SAS–M; Cooper *et al*, 1982); and the Eysenck Personality Inventory (EPI; Eysenck & Eysenck, 1964).

A semistructured interview schedule was used to obtain demographic and social data, and obstetric and psychiatric histories. Also rated were 22 questions concerning attitudes towards pregnancy and childbirth. These were scored as discrete variables on pre-coded scales. Questions included the following: "How happy do you feel about having this baby?"; "Do you have worries about labour and delivery?"; "How confident do you feel about your ability to look after the baby?"

Questions were also asked about social support. Thus, details of the accessibility of family members were collected and three further questions asked: "Do you have someone you can rely on in a crisis?"; "Is there at least one person in whom you can confide?" "Do you feel that you can confide in your partner?"

In assessment (b) (weeks 36–38 of pregnancy), ratings were again made with the PSE, the Montgomery & Åsberg rating scale, and the life events interview. In addition, the women were asked to complete the blues questionnaire on three consecutive evenings. The purpose here was to obtain antenatal 'baseline' blues scores for comparison with later scores in the ten days after delivery. Antenatal ratings were limited to three days in order to maximise the patients' later co-operation in completing the questionnaire on ten post-natal days. For the same reason, women were not asked to complete the Leeds scales or the SAS–M at this assessment.

In assessment (c) (the ten days after delivery), the women completed the blues questionnaire each day, but no other scales.

In assessment (d) (week 12 of the puerperium), the same standardised measures were used as in assessment (a), except that the EPI was not repeated, and questions were added to assess attitude towards the infant.

Detailed information for all patients was obtained from the obstetric case notes on routine procedures and any complications in the index pregnancy, labour, delivery, and puerperium.

Method of analysing scores on the blues questionnaire

As reported in paper I, it was found that there was much individual variation and thus a wide range in the percentage of items on the blues questionnaire which post-partum women endorsed (mean 21.3, s.d. 17.7). For the analysis of discrete variables, such as social class, we defined two blues categories based on the severity of blues scores. A woman was allocated to the first category ('blue 1') if on any day her total score on the blues questionnaire was higher than the *mean peak* score for the whole group of women (that is, the average of all individuals' highest scores). A woman was allocated to the second category ('blue 2') if on any day her total score on the blues questionnaire was higher than the *mean* score for the whole group (that is, the average of all individuals' mean scores). Thus, blue 2 denoted a less severe condition.

For the analysis of continuous variables, such as age, two blues measures were used: the individual's peak score ('bluehigh') and the individual's mean score ('bluemean') over the ten post-partum days.

Results

Numbers of patients

The numbers of patients at the four assessments were (a) 112, (b) 110, (c) 106, (d) 106. The reasons for patients withdrawing were: miscarriage before the second interview (1);

premature delivery (2); admission to special care after delivery (2); and moving away from the area (1).

Blues scores

The numbers of women whose completed questionnaires were satisfactory for analysis were: antenatally, 99; post-natally, 87; both antenatally and post-natally, 79. In this paper, descriptive data are based on the 112 women who were initially recruited, while statistical analyses will be based on the responses of those who completed the blues questionnaire.

Relationships between antenatal and post-natal blues scores

As reported in paper I the mean blues score for all mothers who completed both antenatal and post-natal blues questionnaires ($n=79$) increased from 14.8 antenatally to 21.3 post-natally ($t=2.85$, $P<0.01$), while the mean peak score increased from 23.6 antenatally to 45.7 post-natally ($t=6.08$, $P<0.001$).

The mean total scores of individual women antenatally (mean 14.8, s.d. 15.3) and post-natally (mean 21.3, s.d. 17.7) were significantly correlated with one another (Pearson's $r=0.440$, $P<0.001$). In other words, women who scored highly before childbirth tended to have the higher scores post-natally. Of the 87 women who completed blues questionnaires in the first ten post-natal days, 37 fulfilled the criterion for blue 1, and 52 were allocated to category blue 2, those in blue 1 automatically being included in the blue 2 population.

Social findings

The mean age of the mothers was 28 years (range 16–41 years); most (60%) were aged between 20 and 29 years, while 4% were under 20, 33% between 30 and 39, and 3% over 40 years. Most of the women (92%) were married, 4% were cohabiting, and the rest were single (separated or never married). Nearly half (47%) had a full-time or part-time job. When social class was determined by the method of Goldthorpe & Hope (1974), 72% of the women were deemed to be middle class and 28% working class.

Blues scores were significantly associated with several ratings on the SAS–M completed at weeks 14–16 of pregnancy (Table I). No significant association was found between blues scores and the number or severity of life events reported at either weeks 14–16 or weeks 36–38 of pregnancy.

Obstetric findings

The earlier obstetric history was collected from patients at the first assessment (14–16th weeks of pregnancy). Among the 112 women interviewed, the distribution of earlier experiences was: no previous pregnancy, 40 (36%); one or more miscarriages, 32 (29%); one or more terminations, 10 (9%); still births 2 (2%); medical help for infertility 20 (18%).

When interviewed at the 14–16th weeks of pregnancy, 91 (81%) women said the pregnancy was planned. Among the unplanned pregnancies, half were said to be welcome and half unwelcome.

With one exception, there was no significant association between blues scores in the first ten post-natal days and any item in the obstetric or gynaecological history before the index pregnancy. The one exception was a self-reported history of moderate or severe pre-menstrual tension (13% of the population) which was associated with categories blue 1 and blue 2 (Table I).

Blues scores were not significantly associated with any aspect of the index pregnancy or its sequelae. Thus there were no significant associations with: pregnancy (parity, any complications, number of antenatal visits or hospital admissions); delivery (type of delivery, length of labour, problems such as foetal distress or breech presentation); puerperium (complications such as excessive blood loss, severe tearing, pyrexia, length of stay in hospital); the baby (cord round the neck, jaundice, sticky eye); and feeding the baby (breast or artificial, any feeding problems).

Psychological findings

EPI neuroticism scores at the 14–16th weeks of pregnancy were significantly associated with blues scores in the first ten post-partum days (Table I). There was no significant difference between high EPI scorers and low EPI scorers in their day-to-day variation in blues scores.

Of the attitudes towards pregnancy and childbirth, only fear of labour was significantly associated with any blues measure (Table I).

Psychiatric findings

Of the 112 women interviewed at assessment (a), 28 reported having consulted their general practitioner (GP) at any time in the past because of mood problems.

Among the 72 women who had previously given birth, 18 reported having experienced depression during the post-partum year (three of these having sought medical help, and two having been referred to a psychiatrist). Thirty-seven women reported having definitely experienced maternity blues, while three women reported having probably done so.

In the 12 months before the first assessment, seven women had seen their GP with complaints of emotional symptoms; two of these women had received medication from the GP and two had been referred to a psychiatrist. During the index pregnancy, one woman had seen her GP because of mild anxiety and depressed mood. At the time of the first assessment, none of the mothers was receiving psychiatric care.

At assessment (a), four of the women interviewed were 'cases' on the PSE; at assessment (b), three women were 'cases'. However, at three months post-partum (assessment d), 13 of the 106 women interviewed were PSE 'cases'. Community surveys have indicated that the prevalence of PSE cases in women is around 10% (Surtees *et al*, 1983; Gath *et al*, 1987).

Associations between blues and psychiatric factors

No significant association was found between blues measures in the first ten post-natal days and any history of

TABLE I

Associations between maternity blues and social, obstetric, psychological, and psychiatric factors

	n	'Blue 1'		(% cell values) Blue 1		'Blue 2'		(% cell values) Blue 2		'Bluehigh'		'Bluemean'	
		χ^2	P	*case*	*non-case*	χ^2	—	*case*	*non-case*	*Pearson* r	P	*Pearson* r	P
Social factors													
SAS–M													
poor overal social adjustment	85	—	—			—	—			0.205	*	0.318	***
dissatisfaction with role as houseworker	86	—	—			—	—			0.175	NS	0.194	*
Poor relationship in:													
family unit	63	—	—			—	—			0.204	NS	0.276	*
extended family	84	—	—			—	—			0.256	*	0.329	***
marriage	84	—	—			—	—			0.218	*	0.332	***
Partner a confidante (d.f. = 1):	76	5.05	*			3.80	*			—	—	—	—
is a confidante				2.16	11.8			3.9	10.5				
is not a confidante				51.3	34.2			55.3	30.3				
Obstetric factors													
PMT (d.f. = 1):	56	9.28	**			11.84	***			—	—	—	—
yes				60.7	17.9			64.3	14.3				
no				5.4	16.1			5.4	16.1				
Psychological and psychiatric factors													
EPI neuroticism	87	—	—			—	—			0.337	***	0.419	***
Attitude													
Fear of labour (d.f. = 3):	76	2.93	NS			8.20	*						
marked fear								31.6	23.7				
moderate fear								10.5	2.6				
moderate calm								14.5	5.3				
very calm								2.6	9.2				
PSE case status:													
Time 1	87	0.68	NS			0.86	NS			—	—	—	—
Time 2	87	0.88	NS			1.03	NS			—	—	—	—
Montgomery & Åsberg depression ratings:													
Time 1	86	—	—			—	—			0.307	**	0.274	**
Time 2	86	—	—			—	—			0.300	**	0.280	**
Leeds scale (time 1):													
depression	86	2.40	NS			1.38	NS			0.284	**	0.275	***
anxiety (d.f. = 1)	86	4.6	*			8.53	**			0.287	**	0.399	***
yes				50.0	26.7			53.5	23.3				
no				8.1	15.1			7.0	16.3				

*$P<0.05$, **$P<0.01$, ***$P<0.001$, — no associations can be determined. Cell values for χ^2 analysis are shown for significant associations. The findings summarised here give both significant and non-significant results for psychiatric variables, but only significant associations for social, obstetric and psychological variables.

earlier psychiatric disorder, whether puerperal or non-puerperal.

As shown in Table I, blues measures in the first ten post-natal days were not significantly associated with PSE case status in pregnancy as measured at the first and second assessments. However, both 'bluehigh' and 'bluemean' scores were significantly associated with depression in pregnancy as rated on the Montgomery and Åsberg scales at the first and second assessments. On the Leeds scale (given at assessment (a)) all blues measures were significantly associated with anxiety, while 'bluehigh' and 'bluemean' were significantly associated with depression.

No significant associations were found between blues measures in the first ten post-natal days and any psychiatric measures 12 weeks after delivery.

Subjective recall of the blues

At assessment (d) (week 12 after delivery), the mothers were asked whether, in their view, they had experienced the blues during the first ten days after childbirth, that is, the days during which they were completing the blues questionnaire. Of the 106 women interviewed, 36 recalled experiencing the blues definitely, 33 probably, and 37 not at all.

Of the 69 women who had had definite or probable blues, 62 reported the onset within the first four post-natal days, and 23 of these identified day 3 as the day of onset. Thirty-eight recalled a blues episode lasting only a single day, while 15 recalled a duration of a week or more. All of the 69 women recalled a 'trigger' for the blues, most commonly tiredness, or conflict with hospital staff.

When these subjective reports were compared with scores on the blues questionnaire, there was no significant association between the women who reported experiencing the blues and those who fulfilled the criteria for blue 1 or blue 2.

Discussion

In this study, the main factors positively associated with maternity blues were: poor social adjustment, both overall and within family relationships; poor marital relationships; retrospective history of moderate or severe pre-menstrual tension; high scores on the EPI 'neuroticism' scale; fear of labour; and anxious and depressed mood during the index pregnancy. These findings were generally in agreement with those of earlier published studies.

The finding of an association between the blues and poor family and/or marital relationships is consistent with the findings of Nilsson (1972), Ballinger *et al* (1979), and Cutrona (1983). This is of particular interest because social adjustment was rated six months before the post-natal blues were experienced.

The association found between the blues and the severity of retrospective pre-menstrual tension agrees with the earlier finding of Nott *et al* (1976). This association could point to a biological (hormonal) basis for the blues. On the other hand, both PMT and the blues could be related to a common third factor, EPI neuroticism. In two other studies, complaints of PMT have been found to be highly correlated with EPI neutoricism (Gath *et al*, 1987; Osborn & Gath, 1989). It is important to note that the menstrual data were collected retrospectively and could therefore be unreliable.

In the present study blues scores in the first ten post-partum days were associated with EPI neuroticism measured in the 14–16th weeks of preganancy. Kendell *et al* (1984) also found an association between the two, although in their study the association was particularly with peaking of mood in the post-partum period. On the other hand, it should be noted that neither Pitt (1973) nor Nott *et al* (1976) found any association between the blues and EPI neuroticism.

The finding of an association between the blues and fear of labour during the index pregnancy is consistent with the earlier findings of Davidson (1972) and Stein (1980). Our study also agreed with the studies of Pitt (1973) and Ballinger *et al* (1979) in finding no association between the blues and any other attitude to pregnancy or labour.

Lastly, the present study agreed with several earlier studies (Davidson, 1972; Nott *et al*, 1976; Handley *et al* 1980; Harris, 1980; Stein, 1980) in finding the blues to be associated with mood during the index pregnancy, notably with anxiety and depressed mood.

Turning to the negative findings, no associations were found between the blues and: demographic and social factors (other than social adjustment); life events; obstetric factors; and psychiatric disorder either before or after the index pregnancy. These findings are generally consistent with those of the earlier published studies.

With regard to demographic and social factors, maternity blues was not associated with age, marital status, employment, social class, or social support. In these respects, the blues seems to differ from depressive disorder, which has been found to be related to all these factors (Warheit, 1979; Brown & Harris, 1978). The lack of any association between the blues and life events is consistent with earlier findings (Davidson, 1972; Pitt, 1973; Ballinger *et al*, 1979; Paykel *et al*, 1980; Stein, 1980). Here again, the lack of a positive association seems to differentiate the blues from depressive disorder, which has been found to be related to life events (Brown Harris, 1978; Paykel *et al*, 1969).

There was a notable absence of associ between maternity blues and obstetric factors some workers have reported positive associations between the blues and obstetric factors (Yalom *et al*, 1968; Davidson, 1972), most workers have found no such links.

Perhaps the most important negative finding was the lack of any association between the blues and psychiatric disorder. In the present study, the blues was not related to previous psychiatric disorder, whether puerperal or non-puerperal. The same finding has been reported by most earlier investigators (Yalom *et al*, 1968; Pitt, 1973; Handley *et al*, 1980; Harris, 1980; Stein, 1980). Similarly, we found the blues unrelated to psychiatric disorder 12 weeks after delivery. Two previous prospective studies did find an association between mood in the first few post-partum days and later psychiatric disorder. The explanation may be in the use of different measures in the immediate post-natal period – a measure of depressed mood in one study (Handley *et al*, 1980), and in the other study a visual analogue scale comprising six items (happiness, depression, tears, anxiety, irritability, lability) (Kendell *et al*, 1981).

In the present study, a negative finding with important implications for research method was that the patients' subjective recall of the blues 12 weeks post-partum showed little correspondence with their experience recorded on the blues questionnaire in the first few post-natal days. This finding confirms that collecting blues data retrospectively is unreliable.

In conclusion, the findings could point to a coherent pattern: in predisposed women, the impact of pregnancy and the anticipation of childbirth might induce symptoms of anxiety and depression, together with fear of labour. These symptoms may be worse in women scoring highly on EPI neuroticism or with poor social adjustment. The combination of these factors may increase the incidence or severity of the blues. These psychological and social findings do not preclude biological causes, which could be primary.

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aylor, G. J., *et al* (1979)
ildbirth: clinical findings and
. *Psychological Medicine*, 36,

——, Day, D. S. G., Naylor, G. J., *et al* (1982) Some biochemical findings during pregnancy and after delivery in relation to mood change. *Psychological Medicine*, **12**, 549–556.

Brown, G. W. & Harris, T. (1978) *Social Origins of Depression*. London: Tavistock Publications.

Cooper, P., Osborn, M., Gath, D., *et al* (1982) Evaluation of a modified self-report measure of social adjustment. *British Journal of Psychiatry*, **141**, 68–75.

Cox, J. L., Connor, Y. & Kendell, R. E. (1982) Prospective study of the psychiatric disorders of childbirth. *British Journal of Psychiatry*, **140**, 111–117.

Cutrona, C. E. (1983) Causal attributions and perinatal depression. *Journal of Abnormal Psychology*, **92**, 161–172.

Davidson, J. R. T. (1972) Post partum mood changes in Jamaican women; a description and discussion on its significance. *British Journal of Psychiatry*, **121**, 659–663.

Everitt, B. S. (1974) *Cluster Analysis*. London: Heineman.

Eysenck, H. J. & Eysenck, S. B. G. (1964) *The Manual of The Eysenck Personality Inventory*. London: University of London Press.

Gath, D., Osborn, M., Bungay, G., *et al* (1987) Psychiatric disorder and gynaecological symptoms in middle aged women: a community survey. *British Medical Journal*, **194**, 213–218.

George, A. J., Copeland, J. R. M. & Wilson, K. C. M. (1980) Prolactin in the maternity blues. *British Journal of Pharmacology*, **70**, 102–103.

Goldberg, D. P. (1972) *The Detection of Psychiatric Illness by Questionnaire*. London: Oxford University Press.

Goldberg, D. P., Cooper, B., Eastwood, M. R., *et al* (1970) A standardised psychiatric interview for use in community surveys. *British Journal of Preventive and Social Medicine*, **24**, 18–23.

Goldthorpe, J. H. & Hope, K. (1974) *The Social Grading of Occupations*. Oxford: Clarendon Press.

Hamilton, J. A. (1962) *Post Partum Psychiatric Problems*. St Louis: C.V. Mosby Co.

Handley, S. L., Dunn, T. L., Waldron, G., *et al* (1980) Tryptophan cortisol and puerperal mood. *British Journal of Psychiatry*, **136**, 498–508.

Harris, B. (1980) Prospective trial of L-tryptophan in maternity blues. *British Journal of Psychiatry*, **137**, 223–235.

Jarrahi-Zadeh, A., Kane, F. J., van der Castle, R. L., *et al* (1969) Emotional and cognitive changes in pregnancy and the early puerperium. *British Journal of Psychiatry*, **115**, 797–805.

Johnston, M. (1980) Anxiety in surgical patients. *Psychological Medicine*, **10**, 145–152.

Kendell, R. E., McGuire, R. J., Connor, Y., *et al* (1981) Mood changes in the first three weeks after childbirth. *Journal of Affective Disorders*, **3**, 317–326.

——, Mackenzie, W. E., West, C., *et al* (1984) Day to day mood changes after childbirth: further data. *British Journal of Psychiatry*, **145**, 620–625.

Kennerley, H. & Gath, D. (1986) Maternity blues reassessed. *Psychiatric Developments*, **1**, 1–17.

Levy, V. (1987) The maternity blues in post-partum and post-operative women. *British Journal of Psychiatry*, **151**, 368–372.

Likert, R. (1932) A technique for measurement of attitudes. *Archives of Psychology*, No. 140.

Long Blumberg, N. (1980) Effects of neonatal risk, maternal attitude and cognitive style on early post-partum adjustment. *Journal of Abnormal Psychology*, **89**, 139–150.

Mackay, C. J. (1980) The measurement of mood and psychological activity using self-report techniques. In *Techniques in Psychophysiology* (eds I. Martin & P. H. Venables), pp. 501–558. Chichester: John Wiley & Sons Ltd.

Manley, P. C., McMahon, R. J., Bradley, C. F., *et al* (1982) Depressive attributional style and depression following childbirth. *Journal of Abnormal Psychology*, **91**, 245–254.

MATHEWS, A. & RIDGEWAY, V. (1981) Personality and surgical recovery: a review. *British Journal of Clinical Psychology*, **20**, 243–260.

MONTGOMERY, S. A. & ÅSBERG, M. (1979) A new depression scale designed to be sensitive to change. *British Journal of Psychiatry*, **134**, 382–389.

NILSSON, A. (1972) Paranatal emotional adjustment. In *Psychosomatic Medicine in Obstetrics and Gynaecology* (ed. N. Morris), pp. 157–160. Basel: Karger.

—— & ALMGREN, P. (1970) Para-natal emotional adjustment: a prospective investigation of 165 women. *Acta Psychiatrica Scandinavica* (suppl. 220).

NOTT, P. N., FRANKLIN, M., ARMITAGE, C., *et al* (1976) Hormonal changes and mood in the puerperium. *British Journal of Psychiatry*, **128**, 379–383.

OAKLEY, A. & CHAMBERLAIN, G. (1981) Medical and social factors in post-partum depression. *Journal of Obstetrics and Gynaecology*, **1**, 182–187.

OPPENHEIM, G. (1962) Psychological aspects of pregnancy and childbirth. Lecture to the RMPA quoted by Pitt (1973).

OSBORN, M. & GATH, D. (1989) Psychological and physical determinants of the pre-menstrual syndrome (In preparation).

OWEN, C. Y. & CAMPBELL, E. A. (1987) Maternity Blues: a genuine peaking experience. Paper presented at BPS conference: London.

PAYKEL, E. S., MYERS, J. K., DIENELT, M. N., *et al* (1969) Life events and depression: a controlled study. *Archives of General Psychiatry*, **21**, 753–760.

——, EMMS, E. M., FLETCHER, J., *et al* (1980) Life events and social support in puerperal depression. *British Journal of Psychiatry*, **136**, 339–346.

PITT, B. (1973) Maternity blues. *British Journal of Psychiatry*, **122**, 431–433.

ROBIN, A. M. (1962) Psychological changes associated with childbirth. *Psychiatric Quarterly*, **36**, 129–150.

SNAITH, R. P., BRIDGE, G. W. K. & HAMILTON, M. (1976) The Leeds scale for self-assessment of anxiety and depression. *British Journal of Psychiatry*, **128**, 156–165.

STEIN, G. S. (1980) The pattern of mental change and body weight change in the first post-partum week. *Journal of Psychosomatic Research*, **24**, 165–171.

—— (1982) The maternity blues. In *Motherhood and Mental Illness* (eds P. Brockington & R. Kumar), pp. 119–154. London: Academic Press.

SURTEES, P. G., DEAN, C., INGHAM, J. G., *et al* (1983) Psychiatric disorder in women from an Edinburgh community: association with demographic factors. *British Journal of Psychiatry*, **142**, 238–246.

WARHEIT, G. J. (1979) Life events, coping, stress and depressive symptomatology. *American Journal of Psychiatry*, **136**, 502–507.

WING, J. K., COOPER, J. E. & SARTORIUS, N. (1974*a*) *The Measurement and Classification of Psychiatric Symptoms*. London: Cambridge University Press.

——, ——, —— (1974*b*) *An Instruction Manual for the Present State Examination and CATEGO Programme*. London: Cambridge University Press.

WISHART, D. (1975) *Clustan I.C. Manual*. University College, London: Computer Centre.

YALOM, I., LUNDE, D. T., MOOS, R. H., *et al* (1968) Post-partum blues syndrome: a description and related variables. *Archives of General Psychiatry*, **18**, 16–27.

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Sexual Anxiety in Sexual Dysfunction

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Sexual anxiety was examined in 98 patients presenting with sexual dysfunction and 68 of their partners at a psychosexual clinic using the SOMA questionnaire. All patients had raised values for heterosexual anxiety. Female partners had raised values while male partners did not. This provides further evidence for the role of heterosexual anxiety in the aetiology and treatment of sexual dysfunction.

Sexual anxiety has been implicated in the aetiology of sexual dysfunction by many writers. Masters & Johnson (1970) emphasised the role of 'fears of performance' (or performance anxiety) in both aetiology and maintenance of the problem. Psychoanalytic theory, learning theory, and theories underlying sex therapy have all emphasised anxiety as an aetiological factor (Kaplan, 1982).

Treatments described by various authors emphasise the alleviation of such anxiety. Psychoanalysis holds that the resolution of deep-seated conflicts may relieve anxiety and thus resolve sexual dysfunction (Rosen, 1982). Learning theory focuses on specific circumstances that evoke or maintain anxiety. Many patients show improvement with desensitisation (O'Gorman 1978), social skills training and other techniques that manipulate the negative reinforcement contingencies. Directive therapy involves minimising performance anxiety by avoiding all specific suggestion of goal-orientated sexual performance. This is achieved by taking the couple through a step-by-step programme towards mutually desirable sexual involvement. Kaplan (1982) discusses the use of tricyclic antidepressants and monamine oxidase inhibitors in treatment of women with sexual phobias. She reports improvement with the use of these drugs as "anti-panic medication". It appears that such medication reduces anxiety to the point where directive sex therapy may be of benefit.

The Sexual Orientation Method and Anxiety (SOMA; Patterson & O'Gorman, 1986) is a questionnaire designed to measure sexual anxiety in patients presenting at a psychosexual clinic and is based on the Sexual Orientation Method (SOM; Feldman *et al*, 1966), with additional items relating to sexual anxiety for which the scales were derived from the semantic differential (Marks & Sartorius, 1968). The test scores four components: heterosexual interest, homosexual interest, heterosexual anxiety, and homosexual anxiety. Internal consistency, test–retest reliability, and validity have been demonstrated. It has been shown that patients presenting with sexual dysfunction score high on the heterosexual anxiety component of the SOMA and have low scores on heterosexual interest.

We hypothesised that the partners of such subjects would show similar changes. We also wished to examine the relationship between heterosexual anxiety and the heterosexual interest score in heterosexual subjects. A low heterosexual score might be found in a homosexual subject, in an individual with transient loss of libido, such as might occur in depression, or in an individual with low sex drive.

Method

Ninety-eight consecutive patients presenting with sexual dysfunction at the Psychosexual Clinic in Belfast in 1980 and 1981 were included in the study. It was possible also to include 68 partners (all in heterosexual relationships). Each subject completed the SOMA at presentation. Four groups of subjects were examined: 46 dysfunctional men, 52 dysfunctional women, 41 male partners, and 27 female partners.

The dysfunctional groups included all patients presenting with any form of sexual dysfunction; in the case of men this included erectile and ejaculatory dysfunction as well as disorders of arousal, and in the case of women this similarly included disorders of arousal and orgasmic dysfunction.

Eleven dysfunctional women did not have partners available to complete the questionnaire: in eight cases this was because their partners were unwilling to attend the clinic or to participate in therapy, and in the other three the women had no current regular partner, despite having had at least one recent partner with whom they had attempted sexual intercourse. Nineteen female partners were unavailable to complete the questionnaire: in 12 of these cases the regular partner did not wish to be involved in therapy, in three the dysfunctional male did not wish his partner to attend the clinic and the remaining four had no current regular partner. Dysfunctional men and women whose partners did not complete the questionnaire did not differ statistically from those whose partners did complete the questionnaire on any of the four test scores.

Normal values for men and women have been established by Patterson & O'Gorman (1986).

TABLE I
Heterosexual anxiety and heterosexual scores

	No. of subjects	*Heterosexual anxiety score: mean (s.d.)*		*Heterosexual score: mean (s.d.)*	
Normal men	27	3.93	(3.15)	45.70	(2.45)
Dysfunctional men	46	6.26	(4.48)*	41.50	(6.36)*
Male partners	41	4.15	(3.84)	44.73	(3.22)
Normal women	20	2.30	(3.07)	41.75	(4.20)
Dysfunctional women	52	8.10	(3.94)***	30.90	(12.41)***
Female partners	27	5.81	(3.27)	37.15	(7.18)*

Level of significance compared with normal groups of either sex using Mann–Whitney U test: * $P<0.05$, ** $P<0.01$, *** $P<0.001$.

Results

Table I shows that the male partners of dysfunctional women had heterosexual and heterosexual anxiety scores which did not differ significantly from those of normal men. In contrast the female partners differed significantly from normal women in the heterosexual score. Dysfunctional groups of both sexes differ significantly from their normal counterparts on both scores.

In order to examine the relationship between heterosexual anxiety and heterosexual interest, scores for each subject were plotted (Fig. 1). It was postulated that the relationship would be linear, with heterosexual scores tending to fall as heterosexual anxiety increases. This would be in keeping with the aetiological theories discussed. In fact, both female groups had heterosexual and heterosexual anxiety scores which correlated highly. Spearman rank-order correlation coefficients were -0.81 for dysfunctional women and -0.65 for female partners. Both differences were significant at $P \leqslant 0.001$. The Spearman rank-order correlation coefficients for male partners at -0.13 was not significant and the value for dysfunctional men at -0.27 is significant only at $P \leqslant 0.1$. The plots yield more information.

In fact all individual scores lie at the upper right-hand portion of the graph. A line can be drawn in such a way that only two scores fall below it. This line represents the 98th percentile. The two subjects excluded in this way were both men who presented with sexual dysfunction, specifically primary erectile impotence. Both were married. One patient appeared effeminate and had mild gynaecomastia. His external genitalia were normal. Skull and chest X-rays were normal, as were the electroencephalogram, thyroid function tests, serum testosterone and oestradiol, and semen analysis. Chromosome analysis showed the normal pattern of 46XY. The other patient was noted to appear normal on clinical examination and had normal serum testosterone levels. Neither patient had a raised homosexual score on the SOMA and both denied any homosexual desire or behaviour.

Discussion

Two of the four scores yielded by the questionnaire, SOMA, are examined. The heterosexual component of the score is derived from the SOM, in which six adjectives were chosen from the list provided by Osgood (1957) for their sexual connotations. These are: interesting, attractive, handsome, (beautiful if applied to women), hot, pleasurable, and exciting. Concepts to which these are applied are, "men are sexually to me", and "women are sexually to me". The heterosexual anxiety component used two anxiety scales derived by Marks & Sartorius (1968). These are calm v. anxious and relaxed v. tense. These are applied to the concepts, "men make me feel sexually" and "women make me feel sexually".

Each subject is presented with 112 forced-choice comparisons, such as:

Women make me feel sexually
very anxious ____________________
quite anxious ____________________
Men are sexually to me
neither unpleasurable
nor pleasurable ____________________
very pleasurable ____________________

Patients are instructed to imagine themselves participating in sexual activity with an attractive member of the opposite sex. They are told to tick which of the two statements best describes their present response, and are told that although frequently neither statement will be true, they must mark the one that is closest to their feelings.

Validity of the heterosexual scale has been demonstrated by comparisons of heterosexual and homosexual groups, as well as changes with treatment (Feldman *et al*, 1966). Validity of the heterosexual anxiety scale has been demonstrated by comparisons of various patient groups and by showing improvement after treatment (Patterson & O'Gorman, 1986). In both scales internal consistency has been shown to be high. Eighty per cent of subjects have no or one inconsistency on any ten choice pairs of the heterosexual scale and 77% have no or one inconsistency on any ten choice pairs on the heterosexual anxiety scale. The scoring

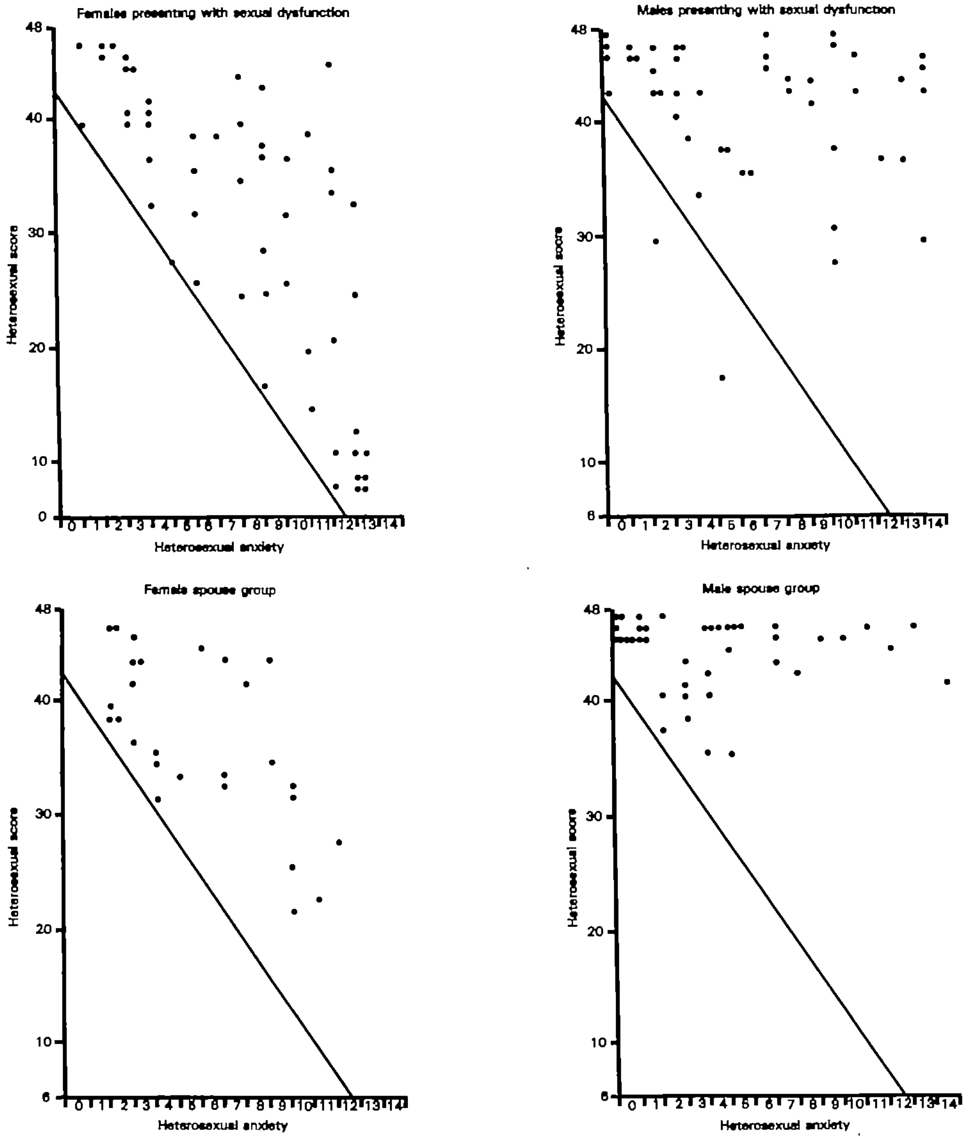

FIG. 1 Heterosexual anxiety and heterosexual scores for the four subject groups.

programme accounts for inconsistencies and can 'correct'. Feldman *et al* (1966) showed that heterosexual inconsistencies tend to decrease after treatment, although this effect was not marked. McCafferty (1984), using a questionnaire of similar construction, showed that subjects with a high number of inconsistencies before treatment tended to have a poorer outcome after treatment. Results must be interpreted bearing in mind the limitations of semantic differential techniques, and the forced-choice procedure.

Figure 1 demonstrates that heterosexual individuals with reduced heterosexual scores on the SOMA invariably have increased heterosexual anxiety. The converse is not true: subjects with increased homosexual anxiety may have normal or slightly reduced heterosexual scores, not falling below the diagonal line shown in Fig. 1. There are three possible reasons why such a definite, linear cut-off occurs on this plot.

(a) Heterosexual anxiety may influence the heterosexual score, tending to cause it to decrease. The degree of such an influence would depend on other factors.
(b) The heterosexual score as it decreases causes the heterosexual anxiety to rise. This effect always operates, but other factors may also cause the heterosexual anxiety to rise.
(c) Some other factor may influence both heterosexual anxiety and the heterosexual score so that as it causes a decrease in the heterosexual score it must cause an increase in the heterosexual anxiety. Other factors may also cause heterosexual anxiety to rise.

The authors have favoured the first of these reasons, as it reflects current theory in that heterosexual anxiety is a strong aetiological or maintaining factor in sexual dysfunction. It is of interest that additional factors must operate to determine the amount of influence that heterosexual anxiety may exert on the heterosexual score. It is possible that time may be one such factor; in other words heterosexual anxiety may be present in an individual for some time before it produces a decrease in the heterosexual score.

Plots of the four diagnostic groups indicate different patterns for each group. The scores for male partners fall in only the upper portion and mostly to the left-hand side of the graph. This group has heterosexual and heterosexual anxiety scores which do not differ significantly from those of normal men (Table I). Dysfunctional men show a wider spread of scores, with a higher proportion falling towards the lower, right-hand portion. This group differs significantly from normal men on both heterosexual and heterosexual anxiety scores.

Dysfunctional women show the most disturbed scores, some scoring the lowest value possible on the heterosexual range. These low heterosexual scores indicate low levels of heterosexual interest but do not imply homosexual orientation. In fact this group, despite having low heterosexual scores, does not have high homosexual scores. These individuals invariably have high heterosexual anxiety scores and probably correspond to the group of phobic patients described by Kaplan (1974). Female partners have heterosexual scores which differ significantly from those of normal women. This difference is in the direction of dysfunctional, although scores are significantly less disturbed than for dysfunctional women. Differences between the dysfunctional women and female partners reach significance levels of $P \leqslant 0.05$ for heterosexual anxiety and $P \leqslant 0.001$ for the heterosexual score.

Masters & Johnson (1970) have described a phenomenon whereby the female partner of a dysfunctional man may develop a high amount of sexual anxiety despite her own apparently normal sexual functioning. The interest in these changes in the direction of dysfunction in female partners lies in the fact that such changes do not occur in the male partners of dysfunctional women. It appears that men are unaffected by dysfunction in their partners, while women react to dysfunction in their partners by developing changes of a dysfunctional nature.

It may be that sexual dysfunction originating in the female partner is an aetiological factor for dysfunction in the man, who eventually presents as the disordered partner. It is difficult, however, to explain why this happens in these cases while the male partners are so remarkably unaffected in their scores by the presence of dysfunction in their partners. One explanation might be that early identification of the sexual difficulty as a problem specifically of the female partner protects the male from sexual anxiety and prevents secondary loss of his sexual interest.

It is of interest that women in a sexually dysfunctioning couple, with dysfunction in either themselves or their partner, tend to have significant decrease in their heterosexual scores. Men in a similar situation have scores much closer to normal values. Feldman *et al* (1966) report lower scores among normal women than normal men in this item of the SOM, but differences do not reach statistical significance. A temporal variant might account for differences noted between dysfunctional men and women: the women might present for treatment at a later stage, thus allowing a greater fall in heterosexual score. However, differences between male and female partners cannot be accounted for in this way. Men may have some inherent factor which prevents a drop in heterosexual interest, even in the presence of dysfunction and heterosexual anxiety. This could be due to a greater capacity of rehearsal of the heterosexual situation in fantasy, allowing sexual interest to be maintained, while not preventing heterosexual anxiety in the real situation. An alternative explanation for this phenomenon is that women tend to remain sexually active despite sexual dysfunction. In this case the woman may learn that sexual activity is unrewarding and may develop loss of heterosexual interest.

The SOMA is of value as a diagnostic tool for dysfunctioning subjects and their partners. It may indicate those patients whose heterosexual interest is decreased in the absence of raised heterosexual anxiety. These patients are unusual and do not appear to respond to standard methods of treatment. The SOMA may enable a better understanding of the nature of heterosexual anxiety and its relationship with heterosexual interest.

References

Feldman, M. P., MacCulloch, M. J., Mellor, V., *et al* (1966) The application of anticipatory avoidance learning to the treatment of homosexuality; III: The sexual orientation method. *Behaviour Research and Therapy*, **4**, 289–299.

Kaplan, H. S. & Novick, A. (1982) The treatment of sexual phobias: the combined use of antipanic medication and sex therapy. *Journal of Sexual and Marital Therapy*, **8**, 3–28.

Marks, I. & Sartorius, N. A. (1968) Contribution to the measure of sexual attitudes. *Journal of Nervous and Mental Disease*, **145**, 441–451.

Masters, W. H. & Johnson, V. E. (1970) *Human Sexual Inadequacy*. Boston: Little Brown.

McCafferty, F. G. (1984) *Sexual Dysfunction in Patients and their Partners*. Thesis for the degree of Doctor of Medicine, The Queen's University of Belfast.

O'Gorman, E. C. (1978) The treatment of frigidity: a comparative study of group and individual desensitization. *British Journal of Psychiatry*, **132**, 580–584.

Patterson, D. G. & O'Gorman, E. C. (1986) A questionnaire measure of sexual anxiety. *British Journal of Psychiatry*, **149**, 63–67.

Rosen, I. (1982) The psychoanalytic approach. Symposium on sexual dysfunction. *British Journal of Psychiatry*, **140**, 69.

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Measuring Behaviour Disorder in Mental Handicap

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By use of latent-trait item analysis (the Rasch model), the internal validity of the behaviour section of the MRC–HBS schedule was analysed. The set of behavioural symptoms in this rating scale was found to measure a one-dimensional structure. Thus addition of item scores provides a meaningful index. Such a numerical measure for the degree of behaviour disorder facilitates comparison between different patients or groups, and furthermore, forms the basis for quantitative description of the outcome of therapeutic intervention. A diagnosis of behaviour disorder was established in 17.2% of 302 mentally-handicapped adults. However, some kind of deviant behaviour was found in 41%, and was correlated with origin and degree of retardation, epilepsy, and place of living. The distribution of the symptoms strongly indicates that organic brain damage is a major aetiological cause.

Behavioural problems are very frequent in the mentally handicapped at all ages and levels of retardation (Corbett, 1979; Jacobson, 1982; Lund, 1985*a*,*b*). Furthermore, these problems are of great importance because they so often interfere with the training, education, and social life of the person. It is, therefore, a major task to prevent and treat such problems. However, before any intervention is started the symptom and its setting should be carefully defined.

The traditional way of measuring behavioural symptoms is by use of a rating scale. A great number of such instruments exist for use in the field of mental handicap. However, the choice is usually rather restricted, because most scales only give a list of ratings for isolated symptoms, without any attempt to reveal general latent or manifest structures for the disorder. Furthermore, the use of many different scales makes the comparison of results rather difficult.

In order to find an instrument for use in an epidemiological study, nine different scales were reviewed (Goldberg *et al*, 1970; Kushlick *et al*, 1973; Ballinger *et al*, 1975; Wing, 1980; Jacobson, 1982; Kazdin *et al*, 1983; Aman *et al*, 1985*a*, *b*; Benson, 1985; Göstason, 1985; Senatore *et al*, 1985; Fraser *et al*, 1986). It was found that the Medical Research Council's schedule of handicaps, behaviours and skills (MRC–HBS), elaborated by Lorna Wing and collaborators (Wing, 1980), was superior because it offers a total description of the person, and covers all levels of mental handicap. The reliability is shown to be good.

Because a diagnosis is defined by symptoms, establishing the diagnosis by quantifying the symptoms from a rating scale into a single index is meaningful only if it can be proved statistically by validity testing that the symptoms form an unequivocal, one-dimensional latent structure (Rasch, 1960). None of the existing scales have been proved to have this property.

The aims of this study were therefore (a) to test the validity of the behavioural part of the MRC–HBS schedule, and (b) to measure the prevalence of behaviour disorder in an epidemiological sample of mentally-handicapped adults.

Method

Study population

By two-stage cluster sampling (Yates, 1981), a group of 324 mentally-retarded adults (age >20 years) was chosen from the register of the Danish National Service for the Mentally Retarded (DNSMR) (Lund, 1985*a*,*b*). At the time of their entry into the DNSMR, the members of the group were living in a part of the county of Aarhus, but at the time of examination 103 (32%) were living outside the sampling area. By comparison of the group with the rest of the adults in the register, no significant difference (at the 5% level) was seen in sex, age (five-year age groups), level of handicap (ICD-8) (World Health Organization, 1974), origin of handicap, or degree of institutionalisation. When examining the group it was found that five members (1.5%) did not fulfil the World Health Organization criteria for mental retardation because they no longer received any special treatment or support. Thirteen refused to join the interview and four were, for practical reasons, out of reach (distance or imprisonment). These 17 (5.3%) who comprised the drop-out group differed significantly from the rest in that they were younger than the average, had a milder handicap and were all living outside institutions.

The remaining 302 members (93%) comprised the study population.

Data collection

The MRC–HBS schedule (Wing, 1980) is a structured interview. The second edition contains 31 sections, 16 dealing with developmental skills and 15 covering items of abnormal behaviour. The items relating to developmental skills are arranged in the order in which the skills appear during the course of normal development. The schedule does not, in the original edition, give an overall score or quotient. Its purpose is to give a profile summarising the levels of performance of different specific skills, and an indication of the number and nature of any behavioural abnormalities. The schedule is a clinical interview, and reliability testing has shown high levels of agreement between trained interviewers (Wing, 1980; Bernsen, 1980).

Sections 28–30 contain twelve items for behaviour problems involving limited or no social awareness (NSA) and five items for behaviour problems with social awareness (WSA). Each item is rated 0 for marked problems, 1 for minor problems or 2 for no problems. On an empirical basis, a matrix for grouping according to the severity of the behaviour disorder has been proposed by Lorna Wing.

The 302 mentally-retarded persons were examined, and their parents or staff members interviewed, in the period 1 December 1983 to 30 May 1984. The total MRC–HBS schedule (second edition November 1978, revised March 1982) was completed for each subject. All examinations and interviews were carried out personally by the author, in the home or institution of the subject.

Statistical analysis

According to Cattel (1973), three major criteria must be fulfilled before a total score is used to represent a combination of items. These criteria are as follows. (a) *Homogeneity* requires that the measure is independent of the part of the scale that has been used to obtain the rating score. (b) *Reliability* refers to the extent to which it may be expected that different observers give the same scores on the same rating occasion; or that the same observer gives the same score on different rating occasions. (c) *Transferability* refers to the extent to which the rating scale measures the same phenomenon in various populations.

Based on comparisons between persons and items, Rasch (1960) has deduced a logistic model with the concepts of homogeneity and transferability built into the analysis, as they are conceived as aspects of the general requirements of objective measurement. Rasch uses the term "*specific objectivity*" when (a) any two people in the study group can be compared, regardless of the questions selected for the comparison (= homogeneity); (b) any two people in the study group can be compared, regardless of who else was included in the study (= transferability); and (c) the comparison is unequivocal. Lack of specific objectivity means that the scoring on a behaviour rating scale cannot be summarised in a single index value (= person parameter).

The Rasch model expresses the probability of person f in reply to item j giving answer k. Denoting this probability by $P\ (f,j,k)$:

$$P(f,j,k) = \frac{exp\ \{[p(f) + i(j)] \times s(k)\}}{n(f,j)}$$

where:

$p(f)$ is the person parameter for person f
$i(j)$ is the item parameter for item j
$s(k)$ is the answer-category parameter for answer-category k
$n(f,j)$ is a constant such that the sum of probabilities for the answering category is 1.

Description of the statistical estimation of the item and person parameters and the testing of the model is beyond the scope of this paper (Rasch, 1960; Allerup & Sorber, 1977; Andersen, 1980; Weinreich & Holmsgaard, 1982). An excellent introduction to the use of latent-trait models in psychiatric epidemiology is given by Duncan-Jones *et al* (1986). However, in general terms, the underlying principle of the Rasch model is to split the sample into two groups, one consisting of persons with predominantly low answers, and the other consisting of persons with predominantly high answers. For each group, a set of item parameters is calculated, expressing the likelihood that the items will produce high answers. If the item parameters for the two groups are in good agreement, this indicates that the items and persons can be characterised on their own, which is the characteristic that makes it meaningful to regard person parameters as a measure of the phenomenon described in the rating scale.

The degree of agreement is evaluated both graphically by drawing the two groups of item parameters against each other, and by a statistical goodness-of-fit test, giving a χ^2 value.

Technical problems in calculating the degree of agreement can occur because the model presupposes at least two answers in all answer categories for each item. In order to test the model in this study, it was necessary to group together minor and major problems. However, there still were a number of items with a distribution of scorings giving less than two answers in each answer category. Therefore, these items had to be discarded.

Details of computer processing are given by Weinreich & Holmsgaard (1982).

In the section on symptoms involving little or no social awareness, items 2–9 were used (items 1 and 10–12 discarded). In the group of symptoms involving social awareness, items 3–5 were used.

The odds ratio (OR) was used as a descriptor of association involving a dichotomous variable. (OR > 1 mean higher prevalence of the variable in the study group than in a control group.) An odds ratio of 2.5 or 3.0 is generally taken to represent the lower limits of strong association. With the odds ratio, 95% confidence limits are presented.

Results

Item analysis

The statistical test for items involving limited or no social awareness (NSA) shows very good agreement with the model ($\chi^2 = 2.34$, 8 d.f., gives $P = 0.97$) (Fig. 1). The test is less good, but still acceptable, for items with social awareness (WSA) ($\chi^2 = 5.17$, 3 d.f., $P = 0.16$). A combined test of the 13 selected items is also accepted by the model ($\chi^2 = 16.74$, 12 d.f., $P = 0.16$). A list of the items, with item parameters, is given in Table I. For the answer category 'minor problems', a value of 0.866 was estimated for WSA items, and 0.846 for NSA items (marked problems being rated 1 and no problems 0).

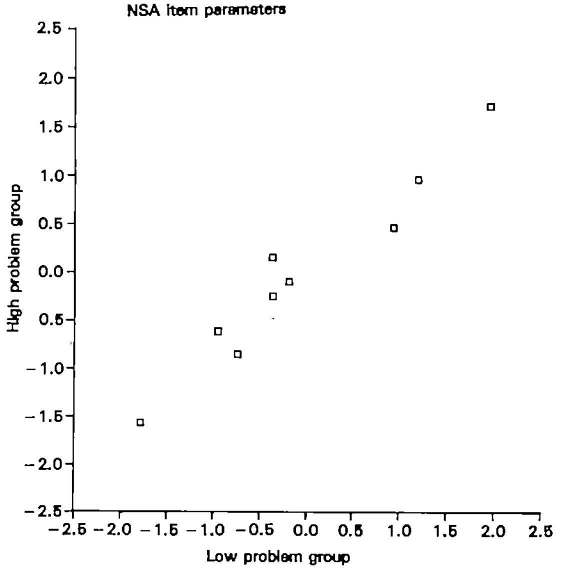

FIG. 1 Item parameters for behaviour problems involving no social awareness (NSA).

Behaviour disorder

Deviant behaviour was found to be very frequent. When all levels were included, 60 men (35.3%) and 59 women (44.7%) were found to present behaviour problems of some kind. The difference between males and females was not significant (χ^2=0.60, OR male=0.8 (1.4–0.5)). However, the majority were just exhibiting one or two minor problems, and only 52 (17.2%) were rated with person parameters over 2.7, which on clinical basis was chosen as the limit for a diagnosis of behaviour disorder. This disorder is most frequently seen in men (OR=1.4 (2.5–0.8)); the prevalence decreases with age and increases with severity of mental handicap. In Table I, the types of behaviour problem are listed according to frequency.

Almost all problems involving limited or no social awareness were significantly more frequent in severely handicapped patients. This correlation was less marked and not significant for problems involving social awareness.

There was a clear correlation between behaviour disorder and epilepsy (Table I). Of the 52 patients with person parameter ≥2.7, 16 ($P<0.01$) were epileptics, 11 ($P<0.0005$) of these having had fits during the last year (Lund, 1985*a*). This correlation was independent of sex, and increased with age (χ^2=10.76, $P<0.005$ for persons over 35 years) and degree of handicap. The present survey

TABLE I

Behaviour problems in mentally handicapped adults, showing correlation with epilepsy and degree of handicap (indicated by odds ratio (OR)), and item parameters (found by Rasch analysis)

	Major or minor problems (%)	*Epileptic fits during last year*	*Severe retardation*	*Item parameters*
		OR (95% confidence limits)	*OR (95% confidence limits)*	
NSA items				
1. Temper tantrums	23.2	2.9 (6.5–1.3)**	5.4 (10.3–2.8)**	–
2. Noisiness	16.6	3.2 (7.4–1.4)**	4.0 (8.2–1.9)**	1.791
3. Destructiveness	11.9	4.2 (10.0–1.8)**	4.3 (10.2–1.8)**	0.973
4. Hyperactivity	9.6	1.3 (4.4–0.4)	7.2 (20.9–2.5)**	0.570
5. Lack of co-operation	6.3	0.6 (4.6–0.1)	6.7 (24.4–1.8)**	−0.734
6. Behaviour in public places	6.0	3.6 (11.2–1.2)*	6.3 (23.5–1.7)**	−0.250
7. Agressive behaviour	5.3	4.2 (13.0–1.4)**	1.6 (4.5–0.6)	−0.485
8. Wandering	3.6	2.6 (12.2–0.6)	2.0 (7.7–0.5)	−0.681
9. Difficult or objectionable personal habits	3.6	4.6 (16.6–1.3)*	7.7 (44.7–1.3)*	−1.184
10. Other behavioural problems	3.0	3.4 (16.1–0.7)	2.6 (12.0–0.6)	–
11. Scatters or throws objects	2.6	–	All severely MH	–
12. Crying and mourning	1.7	–	2.9 (23.1–0.4)	–
WSA items				
1. Difficulties with other people	25.1	1.4 (3.1–0.6)	1.2 (2.4–0.6)	–
2. Rebellious behaviour	19.9	1.3 (3.4–0.5)	1.6 (2.9–0.9)	–
3. Pestering for attention	15.3	3.0 (7.3–1.2)*	1.4 (2.6–0.8)	1.099
4. Lying, cheating or stealing	11.3	3.6 (8.9–1.5)**	1.6 (3.4–0.8)	0.828
5. Other behavioural problems	5.0	1.8 (8.7–0.4)	1.5 (4.7–0.5)	−0.930
Behaviour disorder	17.2	4.5 (10.0–2.0)**	2.2 (4.2–1.2)*	–

* $P<0.05$; ** $P<0.01$.

study gives no information on duration, but reading the case files gave the impression that the various behaviour problems were rather chronic. The connection with epilepsy seems to indicate that organic brain disorder is a major aetiological cause.

Discussion

The pioneer work by Rasch has developed a simple and elegant form of the latent-trait model. This model has been widely used in the development of ability tests, and beginning with Bech (1981), latent-trait methods are becoming an increasingly-used tool for improving measurements in psychiatry (Gibbons *et al*, 1985; Duncan-Jones *et al*, 1986; Goldberg *et al*, 1987).

The latent-trait model provides a mathematical picture of the relationship of the symptoms to the illness. The underlying assumption is that the responses to a particular instrument are all reflections of the single underlying variable that cannot be observed or measured directly. The phenomena of behaviour disorder lend themselves to a dimensional description rather than a categorical model.

The implication of the accepted goodness-of-fit test for the behaviour section of the MRC–HBS schedule is therefore a statistical confirmation of the assumption that the different behavioural symptoms are manifestations of a common underlying mechanism or 'disorder'. The instrument is capable of measuring the manifestations along a continuum because the items comprise a one-dimensional latent structure. The schedule therefore fulfils the conceptual and mathematical criteria for summing the questionnaire data to give a single index, from which a quantitative diagnosis can be established by use of a cut-off point. A single index as a measure of the degree of deviant behaviour is an epistemological advantage, because it permits objective comparison between different patients or groups, and also permits measurement of the outcome of behaviour-modifying interventions such as psychotropic medication, behaviour therapy, or social changes, or combinations of these strategies.

The distinction between symptoms according to degree of social awareness does not reflect any hypothesis of separated diagnostic entities, otherwise the present data set would not fit the Rasch model. However, the individual pattern of manifestations of the common underlying variable does indeed depend on the general level of functioning of the patient. The distribution of the different items (Table I) reveals a raised prevalence of NSA behavioural problems (i.e. involving limited or no social awareness) among more severely retarded patients. This clinical fact makes it meaningful and useful to maintain a division.

Other behaviour schedules might also fit a latent-trait model and thereby document internal validity, but the advantage of the present scale is the fact that it is part of a comprehensive instrument, which offers a total description of handicapped persons of all ages and all levels of retardation.

References

Allerup, P. & Sorber, G. (1977) *The Rasch Model for Questionnaires*. Copenhagen: Danmarks Pædogogiske Institut.

Aman, M. G., Singh, N. N., Stewart, A. W., *et al* (1985*a*) The Aberrant Behavior Checklist: a behavior rating scale for the assessment of treatment effects. *American Journal of Mental Deficiency*, **89**, 485–491.

——, ——, ——, *et al* (1985*b*) Psychometric characteristics of the Aberrant Behavior Checklist. *American Journal of Mental Deficiency*, **89**, 492–502.

Andersen, E. B. (1980) *Discrete Statistical Models with Social Science Applications*. Copenhagen: University of Copenhagen.

Ballinger, B. R., Armstrong, J., Presly, A. S., *et al* (1975) Use of standardised psychiatric interview in mentally handicapped patients. *British Journal of Psychiatry*, **127**, 540–544.

Bech, P. (1981) Rating scales for affective disorders: their validity and consistency. *Acta Psychiatrica Scandinavica*, **64**, Suppl. 295.

Benson, B. A. (1985) Behavior disorders and mental retardation: associations with age, sex, and level of functioning in an outpatient clinic sample. *Applied Research in Mental Retardation*, **6**, 79–85.

Bernsen, A. H. (1980) The children's handicap, behaviour and skills (HBS) schedule. In *Epidemiological Research as Basis for the Organization of Extramural Psychiatry* (eds E. Strömgren, A. Dupont & J. A. Nielsen). *Acta Psychiatrica Scandinavica*, **62** (suppl. 285), 133–139.

Cattell, R. B. (1973) *Personality and Mood Questionnaire*. San Francisco: Jossey–Bass Publishers.

Corbett, J. A. (1979) Psychiatric morbidity and mental retardation. In *Psychiatric Illness and Mental Handicap* (eds F. E. James & R. P. Snaith). London: Gaskell Press.

Duncan-Jones, P., Grayson, D. A. & Moran, P. A. P. (1986) The utility of latent trait models in psychiatric epidemiology. *Psychological Medicine*, **16**, 391–405.

Fraser, W. I., Leudar, I., Gray, J., *et al* (1986) Psychiatric and behaviour disturbance in mental handicap. *Journal of Mental Deficiency Research*, **30**, 49–57.

Gibbons, R. D., Clark, D. C., Cavanaugh, S. V., *et al* (1985) Application of modern psychometric theory in psychiatric research. *Journal of Psychiatric Research*, **19**, 43–55.

Goldberg, D. P., Cooper, B., Eastwood, M. R., *et al* (1970) A standardized psychiatric interview for use in community surveys. *British Journal of Preventive and Social Medicine*, **24**, 18–23.

——, Bridges, K., Duncan-Jones, P., *et al* (1987) Dimensions of neuroses seen in primary-care settings. *Psychological Medicine*, **17**, 461–470.

Göstason, R. (1985) Psychiatric illness among the mentally retarded: a Swedish population study. *Acta Psychiatrica Scandinavica*, **71** (suppl. 318).

Jacobson, J. W. (1982) Problem behavior and psychiatric impairment within a developmentally disabled population – I. Behavior frequency. *Applied Research in Mental Retardation*, **3**, 121–139.

Kazdin, A. E., Matson, J. L. & Senatore, V. (1983) Assessment of depression in mentally retarded adults. *American Journal of Psychiatry*, **140**, 1040–1043.

KUSHLICK, A., BLUNDEN, R. & COX, G. (1973) A method of rating behavior characteristics for use in large scale surveys of mental handicap. *Psychological Medicine*, 3, 466–478.

LUND, J. (1985*a*) Epilepsy and psychiatric disorder in the mentally retarded adult. *Acta Psychiatrica Scandinavica*, 72, 557–562.

—— (1985*b*) The prevalence of psychiatric morbidity in mentally retarded adults. *Acta Psychiatrica Scandinavica*, 72, 563–570.

RASCH, G. (1960) *Studies in Mathematical Psychology – I. Probabilistic Models for some Intelligence and Attainment Tests*. Copenhagen: Danmarks Pædagogiske Institut.

SENATORE, V., MATSON, J. L. & KAZDIN, A. E. (1985) An inventory to assess psychopathology of mentally retarded adults. *American Journal of Mental Deficiency*, 89, 459–466.

WEINREICH, M. & HOLMSGAARD, S. (1982) *User's Guide to the SAS Procedure Raschit*. Copenhagen: University of Copenhagen.

WING, L. (1980) The MRC handicaps, behaviour and skills (HBS) schedule. In *Epidemiological Research as Basis for the Organization of Extramural Psychiatry* (eds E. Strömgren, A. Dupont & J. A. Nielsen). *Acta Psychiatrica Scandinavica*, 62 (suppl. 285), 241–247.

WORLD HEALTH ORGANIZATION (1974) *Glossary of Mental Diseases and Guidance to their Classification*. Geneva: World Health Organization.

YATES, F. (1981) *Sampling Methods for Censuses and Surveys* (4th edn). London/High Wycombe: Charles Griffin.

Jens Lund, MD, *Senior Registrar, Institute of Psychiatric Demography, Psychiatric Hospital in Aarhus, DK-8240 Risskov, Denmark*

KUSHLICK, A., BLUNDEN, R. & COX, G. (1973) A method of rating behavior characteristics for use in large scale surveys of mental handicap. *Psychological Medicine*, 3, 466–478.

LUND, J. (1985*a*) Epilepsy and psychiatric disorder in the mentally retarded adult. *Acta Psychiatrica Scandinavica*, 72, 557–562.

—— (1985*b*) The prevalence of psychiatric morbidity in mentally retarded adults. *Acta Psychiatrica Scandinavica*, 72, 563–570.

RASCH, G. (1960) *Studies in Mathematical Psychology – I. Probabilistic Models for some Intelligence and Attainment Tests.* Copenhagen: Danmarks Pædagogiske Institut.

SENATORE, V., MATSON, J. L. & KAZDIN, A. E. (1985) An inventory to assess psychopathology of mentally retarded adults. *American Journal of Mental Deficiency*, 89, 459–466.

WEINREICH, M. & HOLMSGAARD, S. (1982) *User's Guide to the SAS Procedure Raschit.* Copenhagen: University of Copenhagen.

WING, L. (1980) The MRC handicaps, behaviour and skills (HBS) schedule. In *Epidemiological Research as Basis for the Organization of Extramural Psychiatry* (eds E. Strömgren, A. Dupont & J. A. Nielsen). *Acta Psychiatrica Scandinavica*, 62 (suppl. 285), 241–247.

WORLD HEALTH ORGANIZATION (1974) *Glossary of Mental Diseases and Guidance to their Classification*. Geneva: World Health Organization.

YATES, F. (1981) *Sampling Methods for Censuses and Surveys* (4th edn). London/High Wycombe: Charles Griffin.

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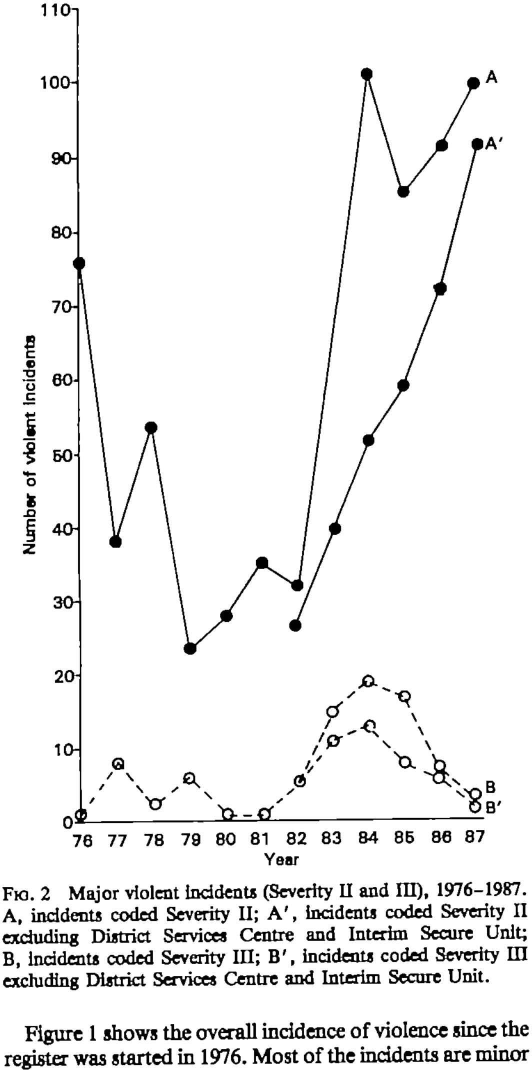

FIG. 2 Major violent incidents (Severity II and III), 1976–1987. A, incidents coded Severity II; A′, incidents coded Severity II excluding District Services Centre and Interim Secure Unit; B, incidents coded Severity III; B′, incidents coded Severity III excluding District Services Centre and Interim Secure Unit.

Figure 1 shows the overall incidence of violence since the register was started in 1976. Most of the incidents are minor (Severity I). The more serious incidents are shown in greater detail in Fig. 2.

There was a progressive increase in violence from the opening of the register in 1976 to a peak in 1984. Some, but not all, of the sharp increase from 1982 to 1984 was attributable to the opening of the two new units. Since 1984 there has been a modest decline.

Method

The violent incidents register was used to identify all the 137 psychiatric in-patients who committed an assault during 1982. The Children's Department, Neurological and Neurosurgical Units, and a regional Interim Secure Unit, were excluded from the study. During 1982 there were 1529 admissions including 568 from the catchment area. Of the patients admitted, 730 were male and 799 female.

The subjects were compared with controls matched for age, sex and ward. The case notes of the subjects and controls were then analysed and rated on 85 clinical and demographic items.

Results

The 137 subjects had committed 470 assaults. Some 65 subjects had committed only one assault, while the remaining 72 subjects were responsible for 405 assaults between them. Where a subject had committed assaults of varying severity the most serious incident was regarded as the 'key incident' for the purposes of the study.

Of the key incidents, 81 (59%) were rated Severity I, 53 (39%) Severity II, and 3 (2%) Severity III. Some of the assaults rated I or II might have been more serious but for the intervention of other staff.

In 92 incidents intervention was solely by ward nursing staff. Medical staff, usually the patient's registrar or the duty doctor, assisted on 43 occasions. Additional help from nursing staff not working on the ward was required on 48 occasions. The police were called on one occasion. Some 70 incidents were dealt with by two or fewer staff, 42 incidents by from three to five staff, and three incidents required intervention by six or more staff. Many incidents disrupted the pattern of work on the ward in addition to any actual injuries sustained.

In most incidents only one person was assaulted. However, two were injured in 19 incidents, three in three incidents, five in one incident, and six in another incident. The use of a weapon was recorded on 19 occasions. Weapons used by men were: table knife, glass tumbler, army helmet, snooker cue, table tennis bat, lighted cigarette, waste paper bin, record player and folded newspaper. Weapons used by women were: handbag, or bag, on five occasions, mug, plaster cast, spectacles, flower vase and shoe..

The most common victims were nurses, who were assaulted on 78 occasions. Other patients were assaulted on 53 occasions, doctors on seven, other staff on seven, and visitors on two occasions.

All three really serious assaults were committed by men, but there was a slight preponderance of women in the other categories, which reflected the preponderance of female admissions (Severity I: female 44, male 36; Severity II: female 30, male 24).

The subjects and controls were closely matched for age. The mean age of patients in the violent group was 36.1 years (s.d. 18.1) and in the control group 36.4 years (s.d. 15.9). These differences are not statistically different (paired t-test = 0.36).

Figure 3 shows the age distribution in detail. Most assaults were committed by young adults, but there was some aggression throughout the entire age range studied.

The monthly totals for the aggressive incidents were: 8 January, 10 February, 11 March, 5 April, 14 May, 16 June, 8 July, 14 August, 11 September, 11 October, 16 November, and 13 December. There is no consistent seasonal pattern.

The daily totals were: Sundays 16, Mondays 21, Tuesdays 28, Wednesdays 18, Thursdays 20, Fridays 23,

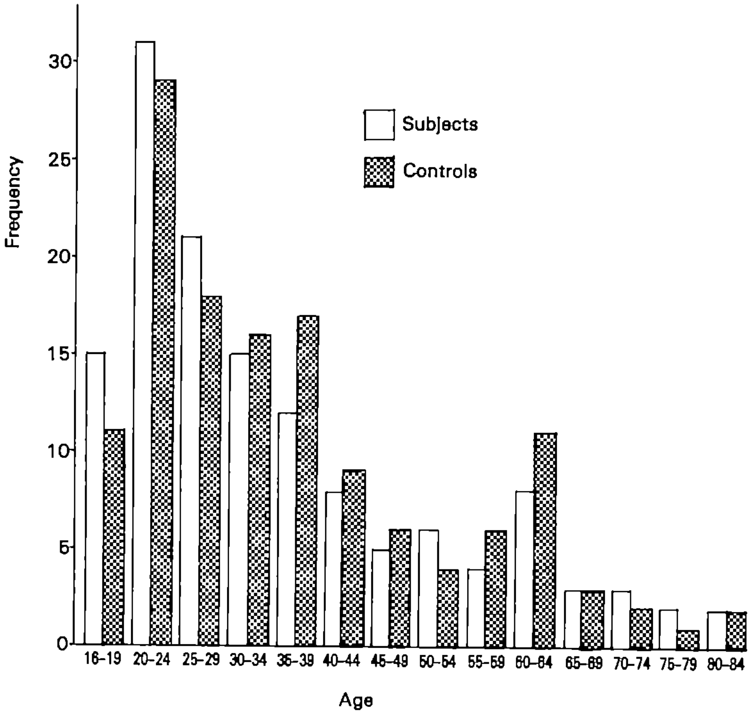

FIG. 3 Age distribution of patients in the violent and control groups.

and Saturdays 11. Fewest assaults occurred on Saturdays and Sundays. The population of patients is reduced by weekend leave and there is less organised activity and staff–patient contact at these times.

Figure 4 shows the 24-hour distribution of aggression. There is an irregular sustained plateau of aggression from 8 a.m. onwards, with a decline towards late evening and little aggression at night. The dip in aggression between 8 and 9 p.m. coincides with the changeover of the day and night nursing shifts.

Clinical features

The primary ICD diagnoses (World Health Organization, 1978) are shown in Table I. Violent patients were more likely to have a primary diagnosis of schizophrenia. Violent patients were also significantly more likely to be hallucinated (violent group 48.9%, control group 36.5%, $\chi^2=5.81$, $P<0.02$) and deluded (violent group 56.2%, control group 43.8%, $\chi^2=4.59$, $P<0.05$).

Of the violent group, 29 patients (21.2%) and of the control group, 26 (19.0%) were admitted formally. There were no clear differences between the groups in the section of the Mental Health Act used.

Taking the whole period of their stay, the violent patients were significantly more likely to be held involuntarily, and in many instances the use of the section order was itself a response to increasingly disturbed or aggressive behaviour.

By the time of the key incident the number in the violent group held formally had increased from 29 to 35. During the total course of the admission 61 patients (44.5%) in the violent group and 32 patients (23.3%) in the control group were held formally at some stage. This difference is highly significant ($\chi^2=16.7$, $P<0.001$). In the violent group, 25 (39.7%) male patients and 36 (48.7%) female patients were held involuntarily at some point during their admission. The corresponding figures for controls are 18 (28.6%) for males and 14 (18.9%) for females.

Previous aggression and antisocial behaviour

Table II shows some behavioural characteristics of the two groups. Damage to property, verbal aggression and threatening behaviour were all markedly and significantly higher in the violent group.

Previous psychiatric admissions

Only 18 patients (13.1%) in the violent group compared with 37 (27.0%) in the control group were the subject of a first admission ($\chi^2=9.0$, $P<0.01$). Some 21 patients (15.3%) in the violent group and 14 (10.2%) in the control group had 10 or more previous admissions. The violent group (mean 4.63, s.d. 4.79) had significantly more previous admissions than the control group (mean 3.60, s.d. 4.42: $t=2.26$, $P<0.05$).

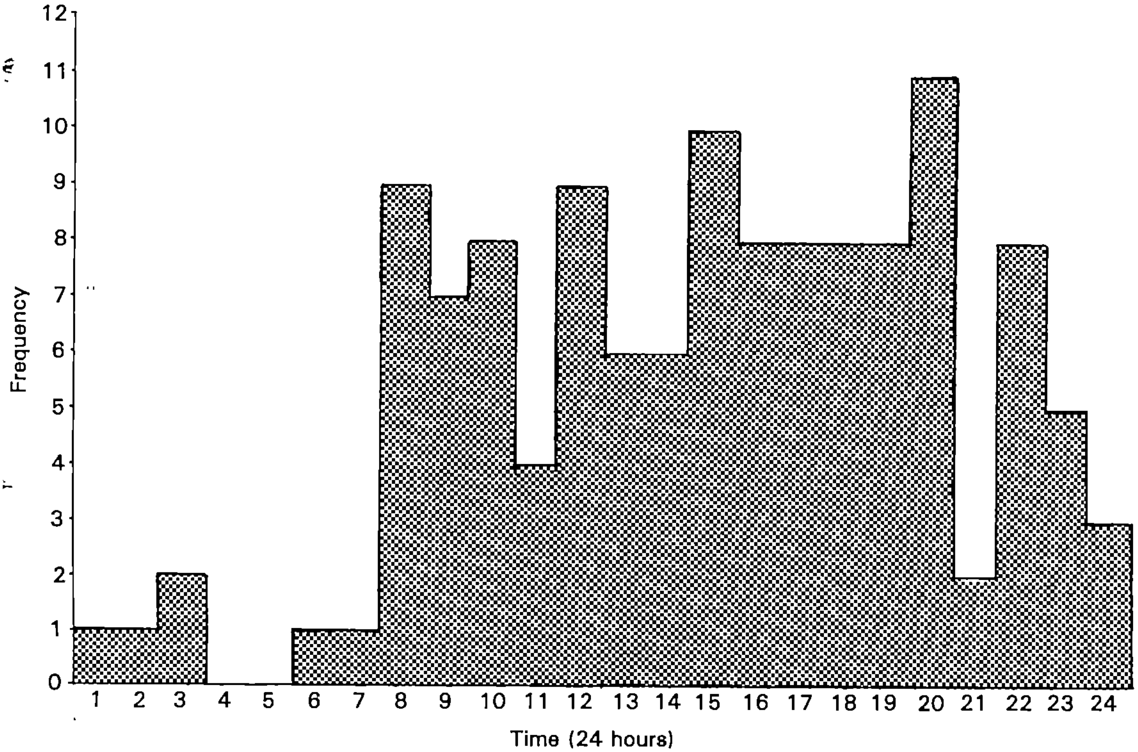

FIG. 4 Distribution of violent incidents over 24 hours for 1976–1987 data.

TABLE I

Diagnostic categories of patients in the violent and control groups

Diagnosis	*Violent group*		*Control group*	
	No.	*%*	*No.*	*%*
Schizophrenia[1]	61	44.5	34	24.8
Depressive psychosis	24	17.5	30	21.9
Mania or hypomania	6	4.4	5	3.6
Unspecified psychosis	1	0.7	4	2.9
Depressive neurosis	5	3.6	4	2.9
Anxiety neurosis	3	2.2	2	1.5
Personality disorder	11	8.0	21	15.3
Drug addiction	0	0.0	2	1.5
Alcohol abuse	1	0.7	7	5.1
Organic psychosis	2	1.5	0	0.0
Senile dementia	3	2.2	4	2.9
Mental retardation/ subnormal	3	2.2	1	0.7
Epilepsy	5	3.6	3	2.2
Other/not known	11	8.0	20	14.6

1. $\chi^2 = 10.8$, $P < 0.01$.

TABLE II

Previous aggressive and antisocial behaviour of patients in the violent and control groups

	Violent group		*Control group*	
	No.	*%*	*No.*	*%*
Previous convictions (non-violent)	27	19.7	22	16.1
Previous convictions (violent)	12	8.8	11	8.0
Damage to property[1,2]	38	27.7	9	6.0
Verbal aggression[1,3]	82	59.8	40	29.2
Threatening behaviour[1,4]	50	36.5	5	3.6
Absconding[1]	35	25.5	33	24.1

1. During index admission.
2. $\chi^2 = 11.64$, $P < 0.001$.
3. $\chi^2 = 25.8$, $P < 0.001$.
4. $\chi^2 = 18.93$, $P < 0.001$.

Social and domestic circumstances

Both groups were socially isolated. Of the violent group, 56.9% were single, 13.1% separated or divorced and only 21.2% were living with a spouse or cohabitee. The respective figures for the control group were 55.5%, 16.8% and 23.5%.

Examination of the work histories indicated that 82 patients (59.9%) in the violent group and 76 (55.5%) in the control group were unemployed at the time of admission. Of the violent group, 69 patients (50.4%), and of the control group, 59 (43.1%), had been unemployed throughout the entire year prior to admission.

Ethnic factors

The hospital serves an inner city area with a substantial immigrant population. Foreign birth was of itself unrelated to violence. Some 30 patients (21.9%) in the violent group and 29 (21.2%) in the control group were born outside the United Kingdom. The 1981 census indicates that 16.6% of the local population of Southwark were foreign born. Information in the case notes was then used to classify the patients into their main ethnic or racial group. The controls comprised: Caucasian 107, Afro-Caribbean 23, other and unrecorded 7. The violent group comprised: Caucasian 89, Afro-Caribbean 35, other and unrecorded 13. Almost all the Afro-Caribbeans were from Jamaica.

Only the Afro-Caribbean and Caucasian groups were large enough for statistical analysis. There were 16.8% Afro-Caribbeans in the control group, compared with 19.8% committing Severity I offences and 33.9% committing Severity II and III offences. The tendency for Afro-Caribbeans to commit more serious violence was significant ($\chi^2=7.23$, $P<0.01$).

Table III compares some clinical and behavioural features of Afro-Caribbeans and Caucasians. There was a tendency for the Afro-Caribbeans to show higher incidences of delusions, hallucinations and schizophrenia, and also more threatening behaviour, and for them to be younger than the Caucasians.

In the violent group 54.3% of Afro-Caribbeans and 39.3% of Caucasians were detained formally at some stage ($\chi^2=2.8$, NS). In the control group 53.3% of Afro-Caribbeans and only 16.8% of Caucasians were detained formally ($\chi^2=13.6$, $P<0.001$). In the violent group 37.1% of the Afro-Caribbean and 15.7% of Caucasians were kept in a locked ward ($\chi^2=10.5$, $P<0.01$). Among controls the difference is even more striking, in that 52.2% of Afro-Caribbeans and 14.0% of Caucasians were in a locked ward ($\chi^2=11.9$, $P<0.001$).

Discussion

A number of studies, including Tardiff & Sweilliam (1982), Health Services Advisory Committee (1987), and Haller & Deluty (1988), have described an apparent increase in violent behaviour by psychiatric in-patients in recent years. The data are often impressionistic and not the result of systematic longitudinal surveys. The Maudsley violent incidents register indicates a substantial increase in violence between the opening of the register in 1976 and a peak in 1984. The increase is not attributable to any overall increase in numbers of beds, which have in fact been reduced slightly during the period studied. The hospital has admitted Section patients and undertaken catchment area responsibilities from 1967. A changing need to deal with more seriously ill and chronic patients and the opening of new units have contributed to the increased levels of aggression. Other general factors are likely to be important. There is an increasing level of violence in society at large, and particularly in the inner city area from which the hospital draws most of its patients. The Health Services Advisory Committee survey (1987) confirms the increasing impact of violence on the work of the Health Service staff, particularly its psychiatric staff.

Systematic data are not available for the period before 1975. However, it was precisely the concern

TABLE III

A comparison of clinical and behavioural features of Afro-Caribbean and Caucasian patients in the violent and control groups

Feature	*Violent group*		*Control group*	
	Afro-Caribbean	*Caucasian*	*Afro-Caribbean*	*Caucasian*
Schizophrenia	18 (51.4%)	36 (40.4%)	9 (39.1%)	25 (23.4%)
Delusions	25 (71.4%)	46 (51.7%)	17 (73.9%)	41 (38.3%)[1]
Hallucinations	25 (71.4%)	37 (31.6%)[2]	17 (73.9%)	31 (29.0%)[3]
Absconding	10 (28.6%)	22 (24.7%)	4 (17.4%)	28 (26.2%)
Damage to property	15 (42.8%)	21 (23.6%)	2 (8.7%)	6 (5.6%)
Threatening behaviour	14 (40.0%)	30 (33.7%)	2 (8.7%)	3 (2.8%)
Verbal aggression	24 (68.6%)	50 (56.2%)	13 (56.5%)	26 (24.3%)[4]
Male sex	18 (51.4%)	40 (44.9%)	15 (65.3%)	47 (43.9%)[5]
Mean age	28.2 (s.d. 16.5)	39.1 (s.d. 17.4)	29.1 (s.d. 10.74)	38.7 (s.d. 16.4)

1. $\chi^2=8.31$, $P<0.01$.
2. $\chi^2=7.00$, $P<0.01$.
3. $\chi^2=14.54$, $P<0.001$.
4. $\chi^2=7.88$, $P<0.01$.
5. $F=2.20$, $P<0.02$.

at an increasingly high level of violence that led to the inception of the register in 1976. Thus what is by today's standards the low level of violence of 1975 almost certainly represents an increase over the levels of previous years.

Encouragingly, levels of violence have decreased moderately since 1984. There has been no material change in the in-patient component of the hospital during that time. The improvement may be a response to a high level of awareness of the problem and improved training of staff.

Nurses have the most daily contact with in-patients, and, as in other studies, they are by far the most commonly assaulted group of staff (Fottrell *et al*, 1978; Fottrell, 1980).

The mean age of the violent patients was 36.1, but there was a considerable spread of violence throughout the age range studied. Tanke & Yesavage (1985) reported no relationship between age and aggression. Fottrell (1980) and Pearson *et al* (1986) reported most aggression in young adults. There is a contrast between the age and sex distribution of psychiatric violence and violence in the community at large, where, overwhelmingly, offenders are young men.

The violent group showed a sigificantly higher proportion of patients with delusions and hallucinations and an increased incidence of schizophrenia which did not reach statistical significance. Other studies, by Fottrell (1980), Tardiff (1981), Pearson *et al* (1986) and Rossi *et al* (1986), have also shown a positive relationship between a diagnosis of schizophrenia and violence. Very few violent patients had a primary diagnosis of organic brain disease, epilepsy, drug addiction, or alcoholism. This is in spite of the fact that the hospital has special in-patient units dealing with these conditions.

Criminal records, family, social and domestic circumstances did not serve to distinguish the violent patients. Unemployment and social isolation were high in both groups. Both groups were characterised by chronic and recurrent illness but the violent group had more previous admissions.

The violent group were best distinguished by their behavioural characteristics during the course of the admission and were rated much higher for damage to property, verbal aggression and threatening behaviour. Aiken (1984), in a study of patients on the hospital's locked Intensive Care Ward, found that 80% of assaults were preceded by changes in the assailant's speech and movement and that changes in posture were significantly associated with serious assaults.

Previous authors have considered the difficulties associated with the prediction of violence in psychiatric patients. Thus Werner *et al* (1983) showed that 15 psychiatrists and 15 psychologists were inaccurate in predicting which of 40 male in-patients would commit assault within one week of admission. Monahan (1984) advocated the development of actuarial techniques with objective demographic data to assist in making clinical judgements.

In this study only 13.1% of the violent patients were on their first admission. Most had several previous admissions. The assaults tended to be repetitive and to be preceded by other clear evidence of aggressive and destructive behaviour. Thus by the time of their key incident the great majority of the violent patients were already well known to the staff and well known to be aggressive. In practice the identification of the potentially violent patient depends most on good communications, good clinical recording, and the ready availability of case notes.

This study was not primarily concerned with racial or ethnic issues. The proportion of Afro-Caribbean patients, particularly in the violent group, is higher than would be expected from a local population survey (Race Equality Unit, Southwark, 1984). The Afro-Caribbeans show a higher incidence of delusions, hallucinations and schizophrenia. Other studies have reported high psychiatric admission rates for Afro-Caribbeans and a disproportionate diagnosis of schizophrenia (Carpenter and Brockington, 1980; Littlewood & Lipsedge, 1981; Cochrane & Bal, 1987).

There was quite a striking association between the race of the patient and the use of restrictive and compulsory measures. This was most marked in the non-violent control group. For instance, in the control group, over 50% of the Afro-Caribbeans were detained formally or detained in a locked ward, compared with only approximately 15% of the whites.

The Afro-Caribbeans tended to be younger, more verbally aggressive, more seriously violent and more psychotic. They are often big and physically strong. These are all factors which contribute to staff apprehension and to the use of restrictive measures.

Other authors have also recorded high compulsory admission rates for Afro-Caribbeans (Ineichen *et al*, 1984; McGovern & Cope, 1987; Moodley & Thornicroft, 1988; Littlewood, 1986; Littlewood & Lipsedge, 1988). The ethnic group of patients in locked wards in other psychiatric hospitals or in Interim Secure Units is not systematically recorded and published. However, the authors' own observations and discussions with colleagues indicate that the proportion of Afro-Caribbeans in such units is much higher than the proportion of Afro-Caribbeans in other psychiatric units or in the population at large.

Possible explanations of the disproportionate psychiatric admission and compulsory treatment of Afro-Caribbeans which have been put forward in the literature include: a genuinely high level of psychotic illness in Afro-Caribbeans, the influence of social and community factors on presentation of illness and distress, the misinterpretation by white psychiatrists of culturally acceptable Afro-Caribbean beliefs, and racial prejudice. We do not intend to enter this debate beyond observing that the issues are clearly of importance for epidemiological research and for the deployment of psychiatric resources, particularly in inner city areas. Particular difficulties do occur in providing good psychiatric care for some Afro-Caribbean patients. It cannot be assumed that a stereotyped service based on the needs of the indigenous inhabitants is necessarily appropriate for all ethnic subgroups.

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We wish to express our appreciation of the many Maudsley Hospital staff who have contributed information to the violent incidents register and, in particular, to express our gratitude to Mr David Russell and Miss Frances Aitken. We also wish to thank Dr Graham Dunn and Mr Charles Sharp of the Institute of Psychiatry Biometrics Department for advice and help in statistical analysis and computer techniques.

References

Aiken, G. D. M. (1982) Personal communication.

—— (1984) Assaults on staff in a locked ward: prediction and consequences. *Medicine, Science and the Law*, **24**, 199–207.

Carpenter, L. & Brockington, I. A. (1980) Study of mental illness in Asians, West Indians and Africans living in Manchester. *British Journal of Psychiatry*. **137**, 201–205.

Cochrane, R. & Bal, S. (1987) The epidemiology of mental illness among immigrants. Paper presented at the Royal College of Psychiatrists' Spring Meeting.

Fottrell, E. (1980) A study of violent behaviour among patients in psychiatric hospitals. *British Journal of Psychiatry*, **136**, 216–221.

——, Bewley, T. & Squizzoni, M. (1978) A study of aggressive and violent behaviour among group psychiatric in-patients. *Medicine and Science and the Law*, **18**, 66–69.

Haller, R. M. & Deluty, R. H. (1988) Assaults on staff by psychiatric in-patients. A critical review. *British Journal of Psychiatry*, **152**, 174–179.

Heatlh Services Advisory Committee (1987) *Violence to Staff in the Health Services*. London: HMSO.

Ineichen, B., Harrison, G. & Morgan, G. (1984) Psychiatric hospital admissions in Bristol. 1: Geographical and ethnic factors. *British Journal of Psychiatry*, **145**, 600–611.

Littlewood, R. (1986) Ethnic minorities and the Mental Health Act; patterns of explanation. *Bulletin of the Royal College of Psychiatrists*, **10**, 306–308.

—— & Lipsedge, M. (1981) Some social and phenomenological characteristics of psychotic immigrants. *Psychological Medicine*, **11**, 289–302.

—— & —— (1988) Psychiatric illness among British Afro-Caribbeans, *British Medical Journal*, **246**, 950–951.

McGovern, D. & Cope, R. (1987) The compulsory detention of males of different ethnic groups with special reference to offender patients. *British Journal of Psychiatry*, **150**, 505–512.

Monahan, T. (1984) The prediction of violent behaviour: toward a record generation of theory and policy. *American Journal of Psychiatry*, **141**, 10–15.

Moodley, P. & Thornicroft, G. (1988) Ethnic group and compulsory detention. *Medicine, Science and the Law*, **28**, 324–328.

Pearson, M., Wilmot, E. & Podi, M. (1986) A study of violent behaviour among in-patients in a psychiatric hospital. *British Journal of Psychiatry*, **149**, 232–235.

Race Equality Unit (1984) *Black and other minorities: Key Facts*. London: London Borough of Southwark.

Rossi, A. M., Jacobs, M., Montelbone, M., *et al* (1986) Characteristics of psychiatric patients who engage in assaultive or other fear-inducing behaviour. *Journal of Nervous and Mental Disease*, **174**, 154–160.

Tanke, E. D. & Yesavage, D. A. (1985) Characteristics of assaultive patients. *American Journal of Psychiatry*, **142**, 1409–1403.

Tardiff, K. (1981) Assault in hospital and placement in the community. *Bulletin of the American Academy of Psychiatry and the Law*, **93**, 33–39.

—— & Swelliam, A. (1982) Assaultive behaviour among chronic psychiatric inpatients. *American Journal of Psychiatry*, **139**, 212–215.

Werner, P. D., Rose, T. & Yesavage, J. A. (1983) Reliability, accuracy and decision-making strategy in clinical predictions of imminent dangerousness. *Journal of Consulting and Clinical Psychology*, **51**, 815–825.

World Health Organization (1978) *Mental Disorders: Glossary and Guide to their Classification in Accordance with the Minor Division of the International Classification of Diseases*. Geneva: World Health Organization.

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Point of View

Hysteria, Belief, and Magic*

DAVID C. TAYLOR

"We cannot command nature except by obeying her" (Bacon)

First, four stories in crescendo.

(a) A courageous GP refers a boy aged eight who has 'gone off his legs' that morning. The GP says he knows it is hysterical but that he cannot stop it. The boy is brought by car. A kind psychiatrist negotiates through the window the need for the boy to mount the steps to come and talk. The boy comes. He talks about how his estranged father had promised first a trip to the cup final and then to the replay and had twice let him down. The anger, love, disappointment, and the humiliation in front of his friends took his legs from under him, turned him weak at the knees, turned his legs to jelly. He walked out of the consultation and remained well.

(b) A 14-year-old boy has a fixed flexion deformity of the right hand. Sudek's atrophy is beginning. The psychiatrist is the 11th sort of specialist to be consulted. A sudden painful inexplicable bruise on the back of the hand has been casually dealt with by a locum GP; after a sleepless night the mother and child waited in casualty for hours, finally to be told that spontaneous bruises were not treated there. The casualty department of an orthopaedic hospital, however, provided a plaster, an appointment to review in two days' time, then admitted him because of pain in plaster, an admission which had lasted for eight weeks before the psychiatrist was called. Several persuasive chats and devices were needed before the hand was able to recover fully.

(c) A very mature 13-year-old girl has twice been admitted for abdominal pain. Following the removal of a normal appendix, anaesthesia develops round the wound and gradually spreads. When encouraged to be upstanding she shows marked astasia abasia. The psychiatrist is called synchronously with a surgeon who, "not going to be caught out", orders a myelogram and a scintillation scan. The family meeting is angrily supportive of the child's right to be ill. The mother works in the medical field, the father is affable but largely absent on business and is said to have a chronic illness, a brother is described as having had an accident in which "he left most of his blood in the road but was otherwise alright", and another brother's school and university careers were ruined by 'lymphoma', which turned out to be spastic colon. Over the ensuing years, despite treatment, the girl works her way through a variety of illnesses including one from which she emerges with the sort of scar she might otherwise have derived from wrist slashing.

(d) A girl of nine vomited her lunch when her sister and boyfriend started to punch one another. The fighting stopped and she was "rushed to hospital". Later, a recurrence of vomiting led to another admission and then one lasting six weeks, needing intravenous fluids. The psychiatrist met her gently mewing into the steel bowl provided. Her trick of deliberate vomiting continued inexorably. Her mother had died of an overdose of drugs and alcohol, her father was a recidivist gaol bird. Both her brothers were in gaol for serious offences. No negotiation with her about her facility to vomit proved possible over 18 months in psychiatric care nor during a subsequent stay at another hospital. There she suffered a rupture of the oesophagus from the stomach and, following a heroic repair, she requested orange juice by mouth. When refused this she made to vomit, reopened her wound, and bled to death.

A number of young people are being presented to doctors with sicknesses of great morbidity and occasional mortality, which ape illnesses or suggest serious diseases, but which are attributed either to unknown or to arcane physical processes by the sick person or his supporters. Doctors, acting on their ordinary assumptions about physical illness, exert themselves and may exhaust themselves in their search for aetiology. In the absence of classic signs, pathognomic illness, or conventional pathological changes, the doctors may then attempt to exit from their engagement, reassuring the patient that all is well, despite the apparent sickness. This reassurance may be accepted, but it may be blocked by the patient or family if they are deeply committed to the sickness in its structural sense (Taylor, 1986; Goodyer, 1986). Even worse, diagnostic frustration or the physician's personal needs might ensnare him into formulations on which reputation is staked and so are not easily relinquished. While it is unarguable that there are yet undiscovered diseases (Slater, 1965), it has also been true throughout the recorded history of medicine that people, transiently or chronically, and for a variety of motives, lay claim to physical ailments, impairments and disorders which they do not have, and for which they are prepared at times to manufacture the evidence. As I see it, such people

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have a belief about how they are, and they are prepared to go to great lengths to make the world congruent with that belief (Robins & O'Neal, 1953; Maloney, 1980; Flechet *et al*, 1983). In children's medicine it is usual for the beliefs to be held by the family, or some part of it, or by some other system, which can include doctors (Goodyer, 1985; Byng-Hall, 1986). Doctors who are not caught up in the system have called these sicknesses deceits (Naish, 1979; Bayliss, 1984) or, more dispassionately or compassionately, hysteria.

There is nothing unreal or imaginary about these sicknesses, even though they are of the imagination, just as the novel or the play is not imaginary although it was imagined. I shall argue that they are an aspect of a defence mechanism, a mechanism which from one perspective we call hysteria but from another perspective we understand as belief, and from another as magic. The dramas of which I gave examples above are mostly chronic socialised medical versions of the hysterical mechanism, which is normally of very rapid onset and offset. I see these dramas as mobilising reactions every bit as powerful as do the more dramatic situations to which I shall later refer.

Belief

I want to draw attention to the fundamental part played in these scenarios by beliefs. Doctors' training is more directed towards what people say and how they act and is too little concerned with what they believe. In a largely godless society, there are few people who experience the power of a benign conviction with which it is easy to empathise. But the mental action of believing, of "accepting propositions as true on the grounds of the testimony of others or on the basis of facts beyond observation" (*Oxford English Dictionary*), while it clearly has survival value, is also subject to abuse. Thus, while it is necessary to have a mental mechanism that allows judgements to be made and action initiated on the basis of incomplete information, such a mechanism does allow false convictions to be arrived at either spontaneously or by the contrivance of others (Taylor, 1987). Included in the definition of beliefs are "propositions accepted on the grounds of evidence", but I do not think really that one can be said to believe in the moon, although one might believe it to be spherical or made of green cheese. Words like 'trust' and 'persuasion' come into belief. Unlike other animals, we can believe what we are told or be persuaded even by that which has not yet been seen and has not yet been directly experienced. We can entertain the notion of terror. Indeed, such a split can be produced within us that, provided we do not believe it, we seek terror for fun. This split between experiential and propositional knowledge, what is true for us against truths of a more empirical sort in the outside world, like "the most beautiful girl in the world" as compared with the height of St Paul's, may be an important component in the sense of conviction, where the individual experiences as propositional and empirical what is actually experiential.

Belief is very carefully treated in psychiatry partly for these reasons and partly because it is essential to respect beliefs, albeit they might seem alien and odd, otherwise psychiatry could claim immense and improper power. Perhaps because of this, the source, impact, and dissemination of beliefs are little studied (but see Jaspers, 1962). People can develop, sometimes quite suddenly, powerful and subsequently incorrigible beliefs (Sargant, 1973). The Christian paradigm is St Paul. These beliefs are not regarded as delusional if they are sanctioned within a relevant social network (Goldberg *et al*, 1987), but they can be damaging to health. Beliefs and normal convictions are the powerful basis of much human behaviour, including illness behaviour.

I shall argue that hysteria, as it presents clinically, arises from deep convictions, avowals, about abnormal states of health or of functioning which are maintained within a small social system about casually selected, if not entirely random, victims who are presented as sick. The characteristics of the victims and the nature of their disorder are the subject of a long debate in medicine (Roy, 1982). However, the characteristics of the victim and the physiology of the disorder may be less crucial to our understanding if we are simply dealing with a medical perspective on an aspect of normal human behaviour, which might be differently interpreted from other perspectives and at other times (Rabkin, 1964; Mayou, 1975; Hurst, 1983).

In 1961 I was house officer to William Sargant. One Saturday he admitted to our ward a teenage girl diagnosed schizophrenic on the evidence of her terrifying sensation of being the victim of systematic persecution by "dark forces" and the fact that an older sister had already been institutionalised for some years, diagnosed with a similar illness. Starting treatment seemed unwise until contact could be made with her parents. Initially, she resisted this, explaining that contact could be made only via intermediaries. As her terror diminished and her confidence grew, she agreed by late afternoon to initiate the contact. Within an hour I was telephoned by her father. He took the view that his daughter had been abducted into hospital by a witches' coven and that he would proceed through public pressure to secure her release. Her fiancé appeared. he was induced, against what he regarded as his better judgement, to reveal to me that the family were extremely secretive because they were in great danger. He instanced

> occasions when his future father-in-law had explained to him the ominous significance of a coil of string in a gutter, a dab of paint on a wall, an ostensibly courteous remark by a waiter. Each was evidence of the malign plot. Armed with this key, a further interview with the patient revealed stories of black rays striking out of clear skies where her father "might have been", and of a Jaguar car hurled to destruction across the M1 which father "could have been driving" had he not, cunningly, been in a small Ford in Devon at the time. The father meanwhile had alerted most of the national press to the incident and telephoned so incessantly that the GPO had to protect the hospital number. Finally, on Monday morning he appeared with his wife, each carrying several large baskets of food and bottled water. To my civil greeting he replied, "You! You are obviously a warlock!" Fortunately, by then I had contacted other agencies who revealed to me that he suffered from schizophrenia, so there were only five and not six participants in this (*folie*) whose beliefs ranged from the delusional through the overvalued to the intense.

The construction we place upon this incident in a psychiatric ward in England, in the late 20th century, is not of a family bewitched, but of a small confined group, powerfully influenced to believe and act upon the basis of a belief held by a schizophrenic, a man suffering a serious chronic disorder of brain function. The rest were in thrall to the power of his conviction. It is a clinical example, but there are abundant political and religious examples that readily come to mind in the world today, and we have the recent history of madmen like Mr Jones, 900 of whose believers were readily persuaded to a synchronous suicide in Guyana.

Hysteria

In its most general sense in medicine, hysteria implies laying claim to, or making an avowal of, bodily dysfunction for which the typical causes are not apparent and in a manner that somehow parodies the sorts of distress produced by organ pathology (Head, 1922; Walshe, 1965). It is dangerous ground for everyone; hysteria might entail pretending by the patient on the one hand, and yet it will also subsume ignorance and error by doctors on the other (Slater, 1965). It has a long history in medicine, which encourages doctors to believe that it is a disease, tangible in some sense (Flor-Henry *et al*, 1981; Flor-Henry, 1985; Guze *et al*, 1986), rather than a description of how things stand between a doctor and his patient, and the patient and his world (Mayou, 1984). Some descriptions of hysteria continue, on the conceit of requiring long-standing claims for sickness in many systems, to portray a syndrome, but hysteria has also to encompass the transient sickness of schoolchildren on a day out. Confusion between hysteria, as that which is being experienced, and hysterics, as those who are experiencing it, has increased the problems in the discourse. Is hysteria something that only hysterics can do? A further problem concerns possible differences between the mechanisms that enable the hysterical response and those that maintain it to a clinical presentation. A conviction might be suddenly arrived at but be abandoned or become incorrigible according to circumstances. The circumstances include the intrapsychic life.

What constitutes hysteria to different doctors is determined by their personal perspective and by their locus in the health care organisation. Psychiatrists mostly see and have written about long-established cases, neurologists have been preoccupied with not allowing themselves to be deceived nor yet overlook organ pathology; both have hankered after running the great neurosis to earth in the neurone. Physicians have leant towards seeing hysteria as a moral flaw or a deceit. Paediatricians, well used to deflecting children's and parents' offers of sickness, are nevertheless sporadically overwhelmed by bravura performances, and then sometimes feel so shy they do not like to let on (Creak, 1938; Dubowitz & Hersov, 1976; Goodyer, 1981; Ernst *et al*, 1984). Almost all doctors, almost all the time, participate in the sexist plot to regard hysteria as a sickness of women, despite the efforts of physicians from as long ago as Briquet and Charcot to the contrary (Owen, 1971), while largely ignoring the massive issue of war-time hysterias.

Very important insights into the probable basis of the hysterical mechanism have come to attention through war-time casualties and through the epidemic hysterias. It is because these occasions recruit so readily from otherwise ordinary human beings that they provide us with a glimpse of possible mechanisms. The arguments about hysteria will continue until the mechanism is clarified. To separate epidemic and war hysterias from clinical cases is simply to evade the issue, at the expense of learning a useful lesson.

The literature on hysteria during and after World War I and II reveals the scale of the problem (Sargant, 1940; Sargant & Slater, 1940, 1941). Thousands of men were affected and, while battle casualties were an important core of the group, much of the hysteria was contributed by non-combatants. Despite an attentive and relatively humane method of dealing with the casualties, they were subsequently largely useless for combat (Slater *et al*, 1941). Considering the extremely detailed, persistent work of the St Louis school and its finding that the male relatives of females with Briquet's syndrome are psychopathic, it is worth noting that many hysterical men were regarded by the military doctors as having been neurasthenic, psychopathic, and shiftless in their pre-military careers. The language of these reports is derogatory in style and condescending, patronising, in flavour. Particular attention was drawn to the model provided for Pavlov by the drowning and near-drowning of his experimental dogs in the Leningrad laboratory flood. The dogs that succumbed to the terror by losing their conditioned reflexes and becoming subsequently untrainable (which must have been annoying to Pavlov) were regarded as having what he called "weak" or "strong excitatory" central nervous systems. "Transmarginal inhibition" was the ambiguous term he applied to the state of brain into which they more easily lapsed than those Pavlov called "lively" or "calm imperturbable" types, which retained their conditioning. Similarly, the war casualties were graded in personality traits, so that groups of men, similar in character to the dogs, could be shown to have behaved similarly under varying degrees of stress. Obviously, invaliding out on psychiatric grounds had to be controlled, and the disparaging language reflects the negative military attitude to the faint of heart. But it suggests too that, for men at least, the option of going transmarginal will be associated with severe loss of esteem whatever the scale of the precipitating event (Sargant, 1973).

In war men came to accept the proposition that they might well die. Often on the evidence of their own eyes, but also on the testimony of others they had, as soldiers, accepted the possibility of death as a fact beyond observation. In other words, they came, at varying degrees of remove from the evidence, to believe they might die. The transmarginal inhibition was a defence. Pavlov believed that ultimately every human being had the capacity for it. Ross (1941), in his interesting short book on war neuroses, quotes from an earlier book by Babinski and Froment in which is a report written by a French medical officer. His report is astonishing.

> "When 'La Provence' was torpedoed we were able to study the manifestations of emotion close at hand apart from any commotional state.
>
> We found that the pithiatic (hysterical) phenomena did not occur until later when the survivors were in safety. These phenomena yielded to an energetic treatment which was immediately applied, and did not recur during the week which followed the accident. Our experience was divided into four periods.
>
> 1st period. On board the boat seventeen minutes between the explosion and the complete disappearance of the boat – period of pure emotion. The crew were anxious and dumb. No cries. Many were in a state of agitation. Later an officer shot himself through the head. This was followed by a small epidemic of suicide. There were however no fits, convulsions or paralyses. In seventeen minutes there was nothing left on the water but wreckage, swimmers and drowned.
>
> 2nd period. In the sea for eighteen hours. Seventeen of us clung to a raft during this period. At first there were some expressions of despair but a cheerful fellow pulled them together by saying he had often been in a much worse hold and was sure he would get out this time. One man began a religious lament which began to upset others, but the officer told him if he did not keep quiet he would throw him in the water. None of the the men died.
>
> 3rd period. After eighteen hours we were picked up by a torpedo boat and when all were on deck I inspected them. Several now showed neuropathic phenomena: quadraplegia, paraplegia, mutism, snarling, weeping, barking, shaking amounting to spasmodic movements of the upper limbs. I sent them down to the engine-room close to the engine where the temperature was very high. The number of my patients increased as new survivors arrived so that out of six hundred picked up there were about forty showing nervous disturbances.
>
> The treatment was simple. They were stripped naked in an overheated room and energetically rubbed by two vigorous sailors with a hair glove soaked in alcohol. As soon as they had been warmed externally and internally with rum, I took each one separately and smacked him harder and harder until the disturbances disappeared, all the time speaking kindly to them and expressing my delight at the rapidity of their recovery. No-one resisted more than ten minutes: many were cured of contagion on witnessing the treatment of the others. The majority expressed to me their gratitude on witnessing the treatment of the others.
>
> 4th period. I was able to see my patients for a week and there were no relapses."

The report describes the traumatic event leading to pervasive stunned shock or a self-destructive alternative. Then, while peril remains but before rescue, a long period of apparent calm. Then, as seen from a medical perspective, some of the phenomena of relief from trauma and peril. Silent tears, congratulatory embraces, gales of laughter are not mentioned, only those men whose 'symptoms' might have some medical connotation, however, various they may be. It is honest about the aggressive nature of the brainwashing treatment. The difference between these symptoms and clinically presented hysterias is that they were experienced by people from a group known to be well only a while before and there are no supporters of their sick condition. Once these circumstances change, the belief, the hysteria, could take a more chronic hold.

Ross's other contribution is to note the paradox of how differently the civilian population, who had ostensibly had the cream of their manhood withdrawn from them, react to the devastation of civilian bombing, from which they can neither escape nor make reprisals, with relatively low rates of hysteria as compared with the troops. Ross wonders whether the deliberate training of military personnel to states of near mindlessness contributes at all to their subsequent breakdown. Of course, the terror and appalling revulsion experienced as a ship is blown up or during the bombardment of soldiers in trenches can only be imagined, but there are accounts of reliving them under abreaction described by Grinker & Spiegel (quoted by Sargant, 1957). This is as near to the moment of the manifestation of the hysterical mechanism as we can get descriptively.

> "The terror exhibited . . . is electrifying to watch. The body becomes increasingly tense and rigid; the eyes widen and the pupils dilate, while the skin becomes covered with a fine perspiration. The hands move convulsively. . . . Breathing becomes incredibly rapid or shallow. The intensity of the emotion sometimes becomes more than they can bear, and frequently at the height of the reaction, there is collapse and the patient falls back in the bed and remains quiet for a few minutes. . ."

Abreaction does not require the reliving of the traumatic event that seemingly precipitated the hysterical symptoms (Shorvon & Sargant, 1947). Its therapeutic value lies in the intensity of an emotional catharsis. It seems to offer a close approximation to the physiology and psychology of the overwhelming event. Sargant (1957) sets this description against one of Wesley's congregation reacting to his hell-fire preaching, and coming to believe through crisis: truly a convert.

Friday 15 June 1739 (Wesley's Journal)

> "Some sunk down, and there remained no strength in them; others exceedingly trembled and quaked; some were torn with a kind of convulsive motion in every part of their bodies, and that so violently that often four or five persons could not hold one of them. I have seen many hysterical and many epileptic fits; but none of them were like these in many respects."

For Wesley, this process, which he called "sanctification", was instantaneous work. It is crucial to my thesis that such depth of conviction is achieved in a moment. Indeed, it is recognised for what it is by its being the work of a moment.

Now consider the mechanism which enables the hysterical response. What would be the biological and evolutionary value of such a mechanism with instantaneous onset and offset? While the response to threat in human beings through flight or fighting back is amply described in student textbooks of physiology and psychology, little is said about responses to events in which these options are both precluded. What options remain? Consider the condition of stunned shock in the bird or the mouse which the cat has caught. They are close to death and maybe, in stupor or even by self-induced death, at least avoid further pain. But there may be a fine margin of profit in playing possum. Several species feign death to deflect potential predators or mimic injury to draw predators away from helpless young. Even the alternative, the frantic, non-cognitive, headless chicken, "violent motor reaction", just *might* secure escape. These two responses were described by Kretschmer (1961) in casualties of World War I, and have been confirmed by others since in wars and disasters. They are seen, albeit at lesser states of intensity, in the classic epidemic hysterias.

The settings of epidemic hysterias, the trigger events, and the symptoms are important to understanding hysteria (McEvedy *et al*, 1966; Moss & McEvedy, 1966; Alexander & Fedoruk, 1986). So too are the nature, quality, and the stridency of the alternative explanations which are always insisted upon a section of the community (usually relatives of victims) which assist in the promotion and maintenance of symptoms (Watson, 1982; Small & Borus, 1983). In these dramas the actors and the audience are equal partners. When the sick are presented to doctors the doctors are compelled to act from their perspective just as the parents or the crowd acted from theirs. In this way the medical procedures tend to validate the sickness to the relatives in the same process which invalidates it to the doctors. Epidemic hysterias arise couched in social settings that enhance emotionality and promote the rapid "mental acceptance of propositions as true even if beyond observations". The sorts of events that produce these responses are unavoidable apparent threats that have emerged through some form of ultra-rapid group consensus. Removal of the affected individuals from the group normally allows them a rapid return to normality since the so-called threat exists much more as a function of corporate than of personal belief. The parallels in animal behaviour are in the extraordinary rapidity of communication in herd and flock behaviour. A recent epidemic of hysteria on the Israel/Arab border, however, was politically exploited, and by precluding appropriate treatment of young people the epidemic persisted longer and spread wider than usual (Hefez, 1985).

> "Thirty-four students . . . were suddenly afflicted by an attack of blindness, headache and stomachache, as well as cyanosis of the . . . limbs. . . . The doctors noticed that two girls had developed complete blindness with respiratory complications and transferred them by ambulance to Affula Central Hospital where they were admitted to the intensive care unit . . ."

Within the affected group in the hysterical epidemic there will be some who are at that moment so placed that, for them, the hysteria is psychologically opportune. This leads to recidivism, as it did in that report, especially if non-symptomatic contacts are keen to exploit the occasion to air their beliefs about aetiology. Currently non-validatable high-technology credos are favoured as bases for these epidemics: viruses, allergens, crop sprays, nuclear fallout, etc. Sadly and tragically, these credos also affect sick children presenting individually whose sicknesses, because they are sporadic, are easily initially misperceived and become even more deeply established as a result of the interventions and investigations required to invalidate medical diagnoses once they have been entertained. In order to make an investigation ethically, the doctor must entertain the same possibility as the complainant, and this reinforces the possibility and it is that which is the important element in the belief.

Magic

Bronowksi (1978) in his *Magic, Science, and Civilization* lectures traces the change in our interpretation of nature from magic to science to the period between 1500 and 1700. He defines magic as "that logic which is separate from the logic everyday life but which, given the secret key, could command nature". Only the initiates would have this power. Of all the situations where people might wish to command nature (such as during drought), sickness, especially in their children, must be the most pervasive and seductive. Since medicine has been largely technologically powerless for most of its history, it is not surprising to find its alliance with magic (Precope, 1954; Maple, 1968). Magical precepts fail, according to Bronowski, as compared with science, in that magic formulae never produce alterations in things at a distance from the magician, except seemingly through the credulity of people. Hence the peculiar fascination of Uri Geller. Where magic formulae succeed they become technology, for example, cinchona bark. According to W. Lehman (quoted by Mauss, 1950, p. 130) "magic derives from errors of perception, illusions and hallucinations, as well as acute, emotive and subconscious states of expectation, prepossession and excitability" and according to Mauss (1950, p. 142) "The magician . . . puts to work collective forces and ideas to help the individual imagination in its belief". Magical cures, then, simply reverse the process of hysterical sickness.

The 'forces' to which Mauss refers are to my view originally in the individual and derive from primitive animism, that historical, but also, and more persistently, developmental phase to which we variably readily regress, and about which we are variably embarrassed when we do. Primitive animism implies that all objects are imbued with their own spirits which have motives, and their behaviour is regulated by the interaction of these spirits, leaving man a hapless bystander, unless he can command them. It is an almost universal experience, especially when we have been let down by a machine. There is thus ample scope for deceit, conviction, and delusion to comingle and interact in manipulating these moments of distorted conviction. If the magical convictions are powerful enough, man can be persuaded to give up life itself (Beecher, 1962; Milton, 1973; Mauss, 1979):

> ". . . the expression on his face becomes horribly distorted. . . . He attempts to shriek, but the sound chokes in his throat, and all that one might see is froth at his mouth. His body begins to tremble and the muscles twist involuntarily. He sways backwards and falls to the ground, and after a short time appears to be in a swoon; but soon after he writhes as if in mortal agony, and, covering his face with his hands, begins to moan." (Basedow,1925, quoted by Cannon, 1942)

This description of death through conviction through "pointing of bones" is compelling similar to the sequence of events in sudden religious conversion, abreaction, war hysteria, and epidemic hysteria, given above. Like the "stunned shock" and "possum" reactions, recovery is immediate if the curse is lifted by the person who imposed it, even when seemingly profound physiological changes have supervened.

More common than such executions are the living deaths or the temporary deaths to which I initially referred. Some of these sicknesses are very long, troublesome and costly; they deserve our attention. They differ from serious diseases by being lived with almost triumphantly, although protestingly, while still maintaining a belief system which conventional medicine does not hold.

In 1985 a 12-year-old boy was referred for a further opinion on management. His parents' view was that he suffered numerous lifelong somatic complaints and, increasingly, behavioural problems which were due to multiple allergies. His allergy to rain had made the national press, but he was also said to be allergic to North Sea gas and a wide variety of other substances, not often thought of as allergens. Initially, he could not be brought into the building where I work because his mother could see that it was the type of building in which potential allergens abound. 'Neutralising drops', available in phials costing £25 each, were used. The touch of these under the tongue instantly enabled him to enter. Nevertheless his 'allergic' response was judged by his mother to be evidenced by his pathetic foul-mouthed observation that she might now leave. He was born, nine years after his only sibling, to an elderly mother. Termination was considered. She suffered from high blood pressure and many 'allergies' that limited her diet. Her husband was a bizarre man of extraordinary social behaviour who had been subject to psychosis from the age of 21. He was still in regular psychiatric care. He also claimed migraine due to potato allergy. Their implacable belief was that their son exhibited lifelong allergy, as evidenced by his having had episodes of sickness and diarrhoea as a baby, his developing stomach pains, weak feelings, muzzy headedness, and his own parody of aggression from his first days at school. They could no longer afford private allergy treatment. They hoped he could be placed in a 'bubble' so that he could recover while protected from the alien world.

The boy, when separated from his parents, was just an obese, dull, unhappy child who reiterated the family beliefs. The parents initially rejected psychiatric treatment and admission to hospital but reluctantly conformed when the question of school avoidance and its legal consequence was raised. He lived for four months in hospital taking ordinary hospital diet and going swimming with the school. No evidence of any form of 'attack' was witnessed except those involving his parents and consisting of childish rudeness and slaps. These were always interpreted by them in terms of reactions to allergens. A consultant paediatrician expert in allergy found only minor traces of evidence, of marginal relevance. Initally, the boy began to settle to the fuller life and improve his impoverished education and social skills. But as pressure to remove him from home more permanently increased, he regressed in his general behaviour, and became firmer in his beliefs about his allergic state. At the same time his father's psychosis decompensated and his mother's beliefs became more fervent and frantic. It became clear that the local authority felt unable to act on behalf of the child on the basis of the available evidence of abuse, and the parents removed the child from hospital. A year later his 'unique problem' made the Sunday newspapers. He was pictured at home, indoors on a rainy summer day. He is the real prisoner of their imaginations.

Levi-Strauss (1967) recognised these sicknesses now being variously labelled by the technologists: he called them "Piteous sicknesses, the total surrender of existence in a last ditch defence of the self by total capitulation."

This capitulation by the organism, often partial, sometimes total, is being hypostatised, made into yet another illness. In hysteria there exists an alternative defence mechanism to fight or flight. It is widespread in animal species. It has an aspect of stupor and an aspect of frantic, mindless activity that is not organised flight. In animals these mechanisms are accessed through extreme terror, usually in situations that imply potential imminent demise. It is crucial that these physiological defence mechanisms unlock instantly if the situation improves. In man the mechanisms are readily accessed in situations of terror, horror, or revulsion, experienced from outside, but in man these states can also be accessed from within, as a result of beliefs. Beliefs are generated by information which is accessed from memory in a subjective (emotional) context. Beliefs differ from certain knowledge in that they are generally arrived at on the basis of partial information and can derive from experiential rather than empirical knowledge. This is not necessarily verbally encoded in memory and is hence inaccessible to verbal approaches. This has survival value but allows error. Belief and false belief are thus tied into the third defence mechanism. In groups it is in the nature of belief to be contagious. Magic plays its tricks through the mechanism of belief.

Sickness evokes aspirations to command nature. In man, through belief, through magic, a mechanism of potentially lethal power can be manipulated. But there are more chronic terrors, more persistent states of being, where neither flight nor fighting back is available. One possible diversion lies in a mechanism which is perceived as sickness, and this at times will be opportune and give rise to lengthy dramas. Unfortunately, doctors cannot guess at that before they become embroiled in them. But they can beware.

References

Alexander, R. W. & Fedoruk, M. J. (1986) Epidemic psychogenic illness in a telephone operators' building. *Journal of Occupational Medicine*, **28**, 42–45.

Bayliss, R. I. S. (1984) The deceivers. *British Medical Journal*, **288**, 583–584.

Beecher, H. K. (1962) Nonspecific forces surrounding disease and the treatment of disease. *Journal of the American Medical Association*,**179**, 437–440.

Bronowski, J. (1978) *Magic, Science, and Civilization*. New York: Columbia University Press.

Byng-Hall, J. (1986) Family scripts: a concept which can bridge child psychotherapy and family therapy thinking. *Journal of Child Psychotherapy*, **12**, 3–13.

Cannon, W. B. (1942) "Voodoo" death. *American Anthropologist*, **44**, 169–181.

Creak, M. (1938) Hysteria in childhood. *British Journal of Children's Diseases*, **35**, 85–95.

Dubowitz, V. & Hersov, L. (1976) Management of children with non-organic (hysterical) disorders of motor function. *Developmental Medicine and Child Neurology*, **18**, 358–368.

Ernst, A. R., Routh, D. K. & Harper, D. C. (1984) Abdominal pain in children and symptoms of somatization disorder. *Journal of Pediatric Psychology*, **9**, 77–86.

Flechet, M. L., Priollet, P., Consoli, S., *et al* (1983) L'oedeme bleu de Charcot. *Annales de Medicine Interne*, **134**, 35–37.

Flor-Henry, P. (1985) Hysteria. In *Handbook of Clinical Neurology*, vol. 2 (46), (eds P. J. Vinken, G. W. Bruyn & H. L. Klawans). Amsterdam: Elsevier Science Publishers.

——, Fromm-Auch, D., Tapper, M., *et al* (1981) A neuropsychological study of the stable syndrome of hysteria. *Biological Psychiatry*, **16**, 601–626.

Goldberg, D., Benjamin, S. & Creed, F. (1987) *Psychiatry in Medical Practice*. London: Tavistock Publications.

Goodyer, I. (1981) Hysterical conversion reactions in childhood. *Journal of Child Psychology and Psychiatry*, **22**, 179–188.

—— (1985) Epileptic and pseudoepileptic seizures in childhood and adolescence. *Journal of the American Academy of Child Psychiatry*, **24**, 3–9.

—— (1986) (Monosymptomatic) hysteria in childhood family and professional systems involvement. *Journal of Family Therapy*, **8**, 1–12.

Guze, S. B., Cloninger, C. R., Martin, R. L., *et al* (1986) A follow-up and family study of Briquet's syndrome. *British Journal of Psychiatry*, **149**, 17–23.

Head, H. (1922) The diagnosis of hysteria. *British Medical Journal*, *i*, 827–829.

Hefez, A. (1985) The role of the press and the medical community in the epidemic of "mysterious gas poisoning" in the Jordan West Bank. *American Journal of Psychiatry*, **142**, 833–837.

Hurst, L. C. (1983) Freud and the great neurosis: discussion paper. *Journal of the Royal Society of Medicine*, **76**, 57–61.

Jaspers, K. (1962) *General Psychopathology* (trans. J. Hoenig & M. W. Hamilton). Manchester: Manchester University Press.

Kretschmer, E. (1961) *Hysteria, Reflex and Instinct* (trans. V. & W. Baskin). London: Peter Owen.

Levi-Strauss, C. (1967) The sorcerer and his magic. In *Magic, Witchcraft, and Curing* (ed. J. Middleton). London: University of Texas Press.

Maloney, M. J. (1980) Diagnosing hysterical conversion reactions in children. *Journal of Pediatrics*, **97**, 1016–1020.

Maple, E. (1968) *Magic, Medicine and Quackery*. London: Robert Hale.

Mauss, M. (1950) *A General Theory of Magic* (trans. R. Brain). London: Routledge & Kegan Paul.

Mauss, M. (1979) A definition of the collective suggestion of the idea of death. In *Sociology and Psychology* (trans. B. Brewster). London: Routledge & Kegan Paul.

Mayou, R. (1975) The social setting of hysteria. *British Journal of Psychiatry*, **127**, 466–469.

—— (1984) Sick role, illness behaviour and coping. *British Journal of Psychiatry*, **144**, 320–322.

McEvedy, C. P., Griffith, A. & Hall, T. (1966) Two school epidemics. *British Medical Journal*, *ii*, 1300–1302.

Milton, G. W. (1973) Self-willed death or the bone-pointing syndrome. *Lancet*, *ii*, 1435–1436.

Moss, P. D. & McEvedy, C. (1966) An epidemic of overbreathing among schoolgirls. *British Medical Journal*, *ii*, 1295–1300.

Naish, J. M. (1979) Problems of deception in medical practice. *Lancet*, *ii*, 139–142.

Owen, A. R. G. (1971) *Hysteria, Hypnosis and Healing: The Work of Jean-Martin Charcot*. London: Dobson Books Ltd.

Precope, J. (1954) *Medicine Magic and Mythology*. London: Heinemann.

Rabkin, R. (1964) Conversion hysteria as social maladaption. *Psychiatry*, **27**, 349–363.

Robins, E. & O'Neal, P. (1953) Clinical features of hysteria in children, with a note on prognosis. A two to seventeen year follow-up study of 41 patients. *Quarterly Journal of Psychopathology*, **10**, 246–271.

Ross, T. A. (1941) *Lectures on War Neuroses*. London: Edward Arnold & Co.

Roy, A. (ed.) (1982) *Hysteria*. Chichester: John Wiley & Sons Ltd.

Sargant, W. (1940) The hyperventilation syndrome. *Lancet*, *i*, 314–316.

—— (1957) *Battle for the Mind*. London: Heinemann.

—— (1973) *The Mind Possessed*. London: Heinemann.

—— & Slater, E. (1940) Acute war neuroses. *Lancet*, *ii*, 1–2.

—— & —— (1941) Amnesic syndromes in war. *Proceedings of the Royal Society of Medicine*, **34**, 757–764.

Shorvon, H. J. & Sargant, W. (1947) Excitatory abreaction: with special reference to its mechanism and the use of ether. *Journal of Mental Science*, **93**, 709–732.

Slater, E. (1965) Diagnosis of "hysteria". *British Medical Journal*, *i*, 1395–1399.

——, Debenham, G., Hill, D., *et al* (1941) Treatment of war neurosis. *Lancet*, *ii*, 107–109.

Small, G. W. & Borus, J. F. (1983) Outbreak of illness in a school chorus. *New England Journal of Medicine*, **308**, 632–635.

Taylor, D. C. (1986) Hysteria, play-acting and courage. *British Journal of Psychiatry*, **149**, 37–41.

—— (1987) Epilepsy and prejudice. *Archives of Disease in Childhood*, **62**, 209–211.

Walshe, F. (1965) Diagnosis of hysteria. *British Medical Journal*, *ii*, 1451–1454.

Watson, N. (1982) An outbreak of hysterical paraplegia. *Paraplegia*, **20**, 154–157.

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Brief Reports

Paedophilia: A Cognitive/Behavioural Treatment Approach in a Single Case

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Our confidence in being able to offer successful treatment of paedophilia remains low. A multifaceted cognitive/behavioural treatment approach is described in the hitherto successful treatment of a man with a 13-year history of sexually interfering with young children of both sexes.

Adams (1980) has noted that the treatment of paedophilia is often difficult. Apart from the strong emotional reactions engendered, many paedophiles see their activities as harmless, and enter treatment at the behest of legal services or to avoid imprisonment.

Despite these facts, a number of papers testify to treatment successes. The technique of covert sensitisation, described in detail later, has been used successfully by Barlow *et al* (1969) to treat paedophilia. Maletzky (1973) demonstrated that the effectiveness of this technique may be enhanced using valeric acid, a non-corrosive foul-smelling substance.

However, the treatment of paedophilia is best seen not only as a reduction of deviant sexual arousal, but also as focused more broadly on other components of deviant social and sexual functioning for the long-term maintenance of treatment effects (Barlow, 1974; Rosen & Rehm, 1977). Examples of such approaches include that of Miller & Haney (1976), who successfully combined aversion conditioning, aversion relief, social and sexual skills training, and supportive psychotherapy. Josiassen *et al* (1980) used multistage aversion and graded social skills training. The treatment programme presented incorporates a number of the behavioural methods of previous studies, but adds an important cognitive dimension to the treatment of paedophilia.

Case report

A 40-year-old man was re-referred to psychiatric services in 1985. Since 1973 he had intermittently been sexually interfering with young children. He had been convicted on two occasions for this.

The client was the youngest and only male of three siblings. He spent much of his first three years in hospital with a blood disorder. He achieved late developmental milestones and was still incontinent at the age of eight. As a child he was physically small, and was bullied throughout school. At the age of seven he was sexually assaulted by a man while in a cinema. Aged 13 he was sexually assaulted by a group of his peers at school.

The client's father was a long-distance lorry driver, absent from the family home for much of the client's youth. He described his mother as very cold and strict.

At 17 the client left home and joined the army. Aged 20, while in Germany, he had his first sexual experience, with a prostitute whom he visited infrequently until his marriage three years later, in 1968. The couple have two boys, born in 1969 and 1972.

In 1973, while posted away from the family, the client first approached a young boy. Following a second approach, to a young girl, he referred himself to an army psychiatrist. The client refused an offer of medication and quickly defaulted from the regular psychotherapy sessions offered him. He continued to interfere with children, including his own, intermittently over the next four years.

In 1977 he first began to approach older children, aged up to about eight years, and had for the first time attempted intromission with a child, who reported him. He was court-martialled in Germany and imprisoned for one year, serving sentence in England. Following his release it was recommended that he seek psychiatric help. He was initially prescribed benperidol, which he was unable to tolerate, and then cyproterone acetate. He found that this had little impact on his behaviour, and he continued to take it while reoffending.

In July 1978, the client was reconvicted. No recommendations were made to the court. The client received a two-year sentence suspended for two years. Over the next seven years the client claims to have been completely free from offence.

In 1982, having previously worked as a storeman, he gained a job as a lorry driver. This work gave him greater autonomy and gradually led him to organising his working day around being present for the schools opening and closing times. Eventually the client reoffended in early 1985 and immediately sought psychiatric help, fearing further imprisonment.

Assessment, treatment and outcome

On initial presentation the client described being eager for a treatment which would eradicate totally any sexual desire towards children. Specifically, he queried the possibility for hypnosis or psychosurgery. Following detailed assessment, four general areas requiring therapeutic intervention were identified.

(a) Extinction of the deviant fantasies and the development of heterosexual fantasy acceptable to the client.
(b) Sex education and therapy.
(c) Cognitive reappraisal: helping the client to examine and rationalise a number of his confused ideas relating to (i) the child offering consent, (ii) the client's notion of guilt, responsibility, and morality, (iii) the implications of his behaviour for himself, his family, and for the children assaulted by him.
(d) Behavioural/environmental control, including increasing the client's confidence and assertiveness with adults, helping him to find alternative employment, offering greater structure and reduced temptation, and helping him to organise spare time to reduce encounters with children during the early stages of therapy.

The client was seen weekly for the first six months of treatment. His motivation for, and compliance with, treatment remained high throughout. Initially, the first two areas described comprised the focus of treatment. The techniques of assisted covert sensitisation and orgasmic reconditioning proved very effective in helping the client to rely less on deviant fantasy to stimulate sexual arousal.

Assisted covert sensitisation requires the client to be guided through the details of his specific fantasies, imagining these scenes as depicted by the therapist. This version imagines the fantasy with the client gradually becoming more and more nauseated to the point of continuous and uncontrollable vomiting within the image. This nausea immediately ceases upon the imagined withdrawal of the deviant arousal stimulus. The foul smell of the valeric acid assists the client's imagination. High expectations are set up for the client feeling nauseous: the client's lap is covered in newspaper and a bucket is placed beside him for his convenience. This procedure was repeated several times at each session for the first four months of treatment and gradually reduced over a further three months.

Orgasmic reconditioning requires the client to masturbate, initially using deviant fantasy, but replacing that fantasy with heterosexual fantasy just before ejaculation. Gradually, the latter fantasy is introduced earlier, until such point as the client can maintain erection and achieve orgasm to the heterosexual fantasy alone. This technique was used similarly before and during intercourse, over a four-month period.

The process of sex education and therapy was conducted jointly with the client's wife. She believed that the client was seeking help for his loss of libido and was unaware of the re-emergence of her husband's real problems. Gradually the couple, both of whom were lacking in basic physiological and behavioural knowledge about sex, were able to increase the frequency of sexual intercourse from once monthly to three times weekly. Standard Masters and Johnson techniques were also used.

The cognitive processes leading to attitude change ranged broadly from the examination and discussion of issues of morality to legal definitions of guilt. The client gradually began to think more rationally, beyond his own experience of having been sexually abused, about the consequences of abuse for the child.

Additionally, helping the client to relive his prison sentence, discussion of the possible abuse of offenders by other inmates, and the effects of reconviction upon his family, all gradually brought home to him the reality of the consequences of reoffence. These attitude changes have remained consistent throughout follow-up meetings.

Finally, behavioural/environmental control involved mixed-group assertiveness training and behavioural target-setting exercises aimed at building confidence. Assertiveness questionnaires (Gambril-Richey, 1975; Rathus, 1973) provided evidence of improvement, as did the client's self-reported confidence in dealing with the public in his new employment as a shop assistant. Free time was spent initially following strict behavioural targets, many of which involved home-based DIY projects. As therapy continued, leisure activities outside the home were encouraged.

After six months, weekly appointments became bi-weekly, then monthly, and currently appointments are six-monthly. In the last four years the client reports no reoccurrence of offences against children and only rarely experiences fleeting deviant fantasy, which he is able to dismiss without difficulty. He and his wife continue to enjoy sex regularly, and he has recently been promoted in his work. Although he continues to feel mildly uncomfortable in the presence of children, these feelings are gradually diminishing.

Discussion

Bradford & Pawlak (1987) highlight a weakness in the present study in their caveat that clients' self-reports in this area are unreliable. However, in routine clinical practice measurements of penile tumescence to deviant stimuli are usually impractical, and questionnaire data offer the same potential for distortion as self-report data. In defence of the specific case presented, there was documented evidence from police and psychiatrists that on direct questioning, and without duress, the client always admitted to a reoffence.

The success of any case of this sort is undoubtedly a function of client motivation. However, the client spontaneously reported that his motivation was born largely out of his being convinced of the logic of the treatment package derived from the assessment. Having re-examined each of the different aspects of treatment at a recent follow-up meeting, the client was asked to rank order the helpfulness of each of the treatment procedures described. He placed covert sensitisation and orgasmic reconditioning equal first. All other procedures he placed equal third. He believed that the first two offered him the initial hope and then the means of altering his paedophilic fantasies, and thus the motivation to comply with and benefit from the other aspects of treatment. He emphasised however that he firmly believed that each of the components of treatment were important at different stages in the therapy.

These findings offer support for the logic of broad-based treatment procedures, and suggest that a cognitive dimension may be used to complement traditional behavioural methods in the management of paedophilia.

References

Adams, H. E. (1980) *Abnormal Psychology*, pp. 350–352. Dubuque, Iowa: William C. Brown.

Barlow, D. H., Leitenberg, H. & Agras, W. S. (1969) Experimental control of sexual deviation through manipulation of the noxious scene in covert sensitization. *Journal of Abnormal Psychology*, 74, 596–601.

Barlow, D. H. (1974) The treatment of sexual deviation: towards a comprehensive behavioural approach. In *Innovative Treatment Methods in Psychopathology* (eds H. E. Adams & K. H. Mitchell). New York: Wiley.

Bradford, J. McD.W. & Pawlak, A. (1987) Sadistic homosexual pedophilia. Treatment with cyproterone acetate: a single case study. *Canadian Journal of Psychiatry*, 32, 22–30.

Gambril, E. D., & Richey, C. A. (1975) An assertion inventory for use in assessment and research. *Behaviour Therapy*, 6, 550–561.

Josiassen, R. C., Fantuzzo, J. & Rosen, A. C. (1980) Treatment of pedophilia using multistage aversion therapy and social skills training. *Journal of Behavior Therapy and Experimental Psychiatry*, 11, 55–61.

Maletzky, B. M. (1973) "Assisted" covert sensitization: a preliminary report. *Behaviour Therapy*, 4, 117–119.

Miller, H. L. & Haney, J. R. (1976) Behaviour and traditional therapy applied to pedophilic exhibitionism: A case study, *Psychological Reports*, 39, 1119–1124.

Rosen, A. C. & Rehm, L. P. (1977) Long term follow up in two cases of transvestism treated with aversion therapy. *Journal of Behavior Therapy and Experimental Psychiatry*, 8, 295–300.

Rathus, S. A. (1973) A 30-item schedule for assessing assertive behaviour. *Behaviour Therapy*, 4, 398–406.

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Musical Hallucinations in a Deaf Elderly Woman

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Musical hallucinations had caused an 86-year-old deaf woman to become anxious and depressed. She was admitted, and tranquillising and hypnotic drugs afforded some slight improvement. The use of her hearing aid to increase ambient noise levels reduced the intensity of the hallucinations, and the patient improved.

References have rarely been made in the English scientific literature to formed auditory hallucinations related to acquired peripheral deafness (Colman, 1894; Rhein, 1913; Rozanski & Rosen, 1952). Ross *et al* (1975) presented two further cases, both with musical hallucinations, and commented that all the described cases conformed to an almost stereotyped pattern. We report a further case.

Case report

An 86-year-old married woman was admitted to our unit with a two-month history of increasing anxiety, agitation, and restlessness, and constant depression with loss of interest, insomnia, poor appetite, and early morning wakening. She complained bitterly that she had been hearing music for the previous nine months. Its onset had been sudden, and she thought that it had first occurred after underoing audiometry and wax aspiration at an ENT outpatient clinic.

The hallucinations consisted of an unaccompanied and unknown male baritone voice singing melodies either to 'la la' or to the words of traditional Scottish folk-songs. She heard them with her left ear only, describing the sounds as being located at times within her ear, and at times outwith her body. They were annoyingly repetitive: lines or verses repeated over and over again, the songs occasionally being sung *in toto*. They were fairly constantly heard, with infrequent short pauses, could not be stopped or altered by the patient, and were more intense at night and at other quiet times. They decreased in intensity with her (left) hearing aid *in situ* and switched on.

The patient was fully aware of the hallucinatory nature of her experiences. She was only marginally temporarily disorientated, with a moderately poor short-term memory, an inability to perform complex arithmetical subtractions, and a poor knowledge of current affairs. There was no previous psychiatric history or relevant family history.

The patient was the youngest in a family of five children and was raised at home by her parents, both jute workers. She left school aged 14 to enter the jute industry and married at 20. The union was happy but childless. She retired from full-time work at 60 but continued to work as a home-help for another 10 years. Her husband was killed in a traffic accident when the patient was aged 67 and she remarried aged 73, her second husband being 15 years younger. Some five years previously they had moved to their present abode.

Total deafness, of unknown cause, had been present in her right ear since early childhood. For the past 20 years she had experienced tinnitus and increasing perceptive deafness on the left side. Two years before admission she had been issued with a hearing aid.

At age 67 she sustained a head injury, with a five-minute loss of consciousness, and had post-traumatic amnesia, of uncertain duration, from which she made an uncomplicated recovery.

Routine general physical examination was unremarkable. The patient exhibited a degree of ambidexterity, but the right hand was considered to be dominant. There was no left handedness in the family. Neurological examination was normal, except that some nominal dysphasia was exhibited, in particular with increasingly uncommon objects (for the patient, e.g. a drawing pin), and she confabulated when identifying these. Drawing a clockface from memory caused some problems and was abandoned. There was, however, no evidence of visual field neglect. Some difficulties in spatial orientation were also noted, with the patient inverting the arrowheads in drawing a series of parallel arrows, in all the cardinal directions. A slight, but inconsistent, right–left disorientation was manifest on tests of finger agnosia.

On the Kendrick Battery both object-learning and digit-copying scores were low (age-scaled quotients = 70 and 60 respectively), placing the patient in the dementing category. A design could not be drawn correctly from memory on the Benton Visual Retention Test, again suggestive of a significant deficit. With both these tests there were some perseverative responses. Further drawing tests suggested diffuse impairments in functioning.

Routine haematological and biochemical investigations were normal. TPHA was negative. Chest X-ray showed cardiomegaly and signs consistent with incipient cardiac failure. Skull films revealed increased right frontal bone density, but computerised tomography (CT) showed only a minor degree of generalised cerebral atrophy. An EEG produced a low-amplitude, poorly rhythmic recording, and there was evidence of right hemisphere dysfunction involving mainly the frontotemporal area.

ENT examination confirmed the existing hearing loss but could detect no new pathology.

The patient was treated with thioridazine in low, divided dosage (25 mg thrice daily) and a short-acting benzodiazepine hypnotic (temazepam 10 mg) with some little improvement. The use of her hearing aid on the affected side, with an increase in ambient noise levels, resulted in a marked decrease in her hallucinosis and on discharge, seven weeks after admission, her agitation and dysphoria had settled. Follow-up in the community, six months after discharge, revealed that the patient was physically well. She remained active and affectively settled and was continuing to use her hearing aid. She reported her hallucinations still present but less bothersome.

Discussion

The history presented by our patient conformed closely to the almost stereotyped pattern described by Ross *et al* (1975), Miller & Crosby (1979) and Hammeke *et al* (1983) of highly organised, vivid and intricate musical hallucinations consisting of a voice or voices, or an instrument, band or orchestra, which almost always reflect past musical memories. Such hallucinations are generally preceded by a long history of progressive unilateral or bilateral sensorineural deafness together with tinnitus, are experienced predominantly in the deaf or deafer ear, and are often of acute onset at a time of a further decrement in hearing. The ear or head is commonly named as the site of supposed origin. Most patients seem to hear a repetition of the same melody or melodies, which begins on awakening and continues throughout the day. Awareness of the music varies with the sufferer's attentiveness, being intensified by mental inactivity and with low ambient noise levels. They can be very disturbing, but are sometimes pleasing, with the patient harmonising or singing along. In the cases described by Miller & Crosby (1979) and Hammeke *et al* (1983), the patients were able consciously to alter the tune or its speed or volume.

Our patient's EEG and CT findings echo those of Miller & Crosby (1979) and Hammeke *et al* (1983), whose patients all showed EEG evidence of abnormalities in the temporal regions, and in whom CT revealed findings of mild diffuse cerebral atrophy. Neuropsychological testing in our patient, although not exhaustive, suggested diffuse impairments in functioning similar to those found by Hammeke *et al* (1983), one of whose patients showed evidence of mild, probably diffuse, cerebral dysfunctioning with impairment in memory and learning tasks.

In none of the reported cases have these hallucinations been associated with a psychosis or a previous history of mental illness.

There is disagreement about the possible anatomical substrate for the phenomenon. Rozanski & Rosen (1952) state that musical hallucinations have been described in various organic diseases, including tumours and vascular lesions, involving the temporal lobe, as well as in epilepsy, diffuse cerebral diseases, and in drug-induced intoxicated states. They are at pains to point out, however, that cerebral disorders seem to play no part in the causation of their patient's condition which, they assumed, arose from pathological changes of the aural end-organ alone and they cite, as a point of differentiation, the paroxysmal nature of the hallucinations in the formed conditions compared with the persistent nature of them in the latter. Ross *et al* (1975) hold to this view, citing similar phenomena produced by other end-organ disease, in particular visual hallucinations associated with blindness – the Charles Bonnet syndrome. Their main postulate is that the formed hallucinations result from distortions in the normal processing of sensory information so that abnormal perceptions occur centrally, and that such distortion need not imply neuronal damage.

Hammeke *et al* (1983), in discussing these views, use the construct of 'sensory deprivation' as the primary neurophysiological mechanism so that normally, sensory input is said to suppress much non-essential information but, in conditions of reduced sensory input, disinhibition of perception-bearing circuits may occur, thereby 'releasing' perceptual traces, including previously acquired memories, which are then re-experienced. Other investigators, they say, argue for a combination of peripheral and central dysfunction, supported by the fact that these hallucinations are shown to occur most frequently in an elderly population. Direct evidence of central dysfunction is provided by EEG abnormalities in the majority of cases studied, CT abnormalities in all cases studied, and neuropsychological abnormalities in their own patients. In support, our patient has abnormal findings in all these spheres also. Whether this dysfunction is central to, contributory, or coincidental to the phenomenon is as yet unknown.

Although rarely reported, Ross *et al* (1975) predicted that the incidence of this disorder might well be higher than generally appreciated since patients' self-reports were low because of the fear that the symptom might suggest psychiatric disorder. This prediction was found to be correct (Ross, 1978).

Interestingly, although our patient was unable to alter or abolish her hallucinations consciously, the use of her hearing aid to increase the ambient noise level resulted in better control and tolerance of her hallucinosis and this echoes the experiences of other patients who could suppress their hallucinations by playing the television or radio loud. Nevertheless, this result may be fortuitous since a measure of tolerance to the experience seems to develop in time (Ross, 1978). In our own experience and that of Miller & Crosby (1979), there would seem to be a place for pharmacological treatment using tranquillising or hypnotic drugs. However, Hammeke *et al* (1983) report that anticonvulsant, antipsychotic, and vitamin supplement therapy fail to produce major benefits.

References

COLMAN, W. S. (1894) Hallucinations in the sane associated with local organic disease of the sensory organs, etc. *British Medical Journal*, *i*, 1015–1017.

HAMMEKE, T. A., MCQUILLEN, M. P. & COHEN, B. A. (1983) Musical hallucinations associated with acquired deafness. *Journal of Neurology, Neurosurgery and Psychiatry*, 46, 570–572.

MILLER, T. C. & CROSBY, T. W. (1979) Musical hallucinations in deaf elderly patients. *Annals of Neurology*, 5, 301–302.

RHEIN, J. H. W. (1913) Hallucinations of hearing and diseases of the ear. *New York Medical Journal*, 97, 1236–1238.

ROSS, E. D., JOSSMAN, P. B., BELL, B., *et al* (1975) Musical hallucinations in deafness. *Journal of the American Medical Association*, 231, 620–621.

ROSS, E. D. (1978) Musical hallucinations in deafness revisited. *Journal of the American Medical Association*, 240, 716.

ROZANSKI, J. & ROSEN, H. (1952) Musical hallucinosis in otosclerosis. *Confina Neurologica*, 12, 49–54.

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Social Phobia Secondary to Pathological Sweating

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An individual with agenesis of the corpus callosum associated with recurrent severe sweating and hypothermia developed a social phobia. Phobias may be adaptations to real and potentially dangerous physiological events.

Agenesis of the corpus callosum in association with recurrent hypothermia and attacks of sweating and chills, also known as Shapiro's syndrome, is a rare disorder whose psychiatric sequelae have yet to be reported (Shapiro *et al*, 1969; Noel *et al*, 1973). The cause of the recurrent hypothermia is unclear. The case we report here is of a man with agenesis of the corpus callosum whose hypothermia was not recurrent, as it has been in most previously reported cases (Johnson & Jones, 1985), but was constant. Eventually, severe sweating in times of emotional stress led him to avoid certain social encounters in which others might scrutinise him.

Case report

The patient had a normal course until the age of 19, when he developed severe sweating attacks that would lower his core body temperature 3 °C or more at a time. Simultaneously, he lost the ability to keep his body temperature within normal range. In his early 20s, he spent a total of three years as an in-patient at the National Institute of Health, during which time his temperature would sometimes drop as low as 21 °C, and he suffered frequent attacks of status epilepticus. His seizures were felt to be secondary to his very low temperature. Except for diffuse slowing at times of low temperature, his EEG was normal, and he never showed any clinical evidence of the syndrome of complex partial seizures. His seizures and to some degree his hypothermia were finally controlled on phenobarbitone (180 mg) and cyproheptadine (12 mg) daily, allowing him to leave the hospital. However, he found work difficult, as excessive sweating would result in drops of body temperature, with accompanying cognitive deficits.

He entered our out-patient psychiatric clinic complaining that he could not find a girlfriend. When first seen by us, he still had difficulty controlling his temperature. He would wake up in the morning with his temperature in the high 20s °C, and then take a series of hot baths to increase his temperature to over 30 °C, when his ability to speak coherently or do simple calculations would improve appreciably. However, if his temperature fell below 30 °C, he experienced cognitive deficits and generalised weakness.

A gregarious individual before the onset of illness, the patient remained sociable for some years. Occasionally, he suffered sweating attacks for no apparent reason. However, some years after his long period in hospital, he began to note that emotional stress would sometimes precipitate such attacks, something which had never occurred in hospital. Within a period of five to ten minutes, he would sweat so much he often lost up to 2 kg body weight, while his temperature might decrease 3 °C or more. When he finally stopped sweating, he became exceedingly sluggish, and was unable to function mentally or physically. He began to fear the recurrence of seizures if the sweating attacks became too severe. The emotional stressors that provoked the sweating were going out with women and queuing to pay in cafeterias or shops, situations where he could feel people were watching him.

The patient was seen in group and individual therapy. In group therapy, he would sometimes feel 'emotional' and start to sweat. Embarrassment at his appearance, and the further scrutiny he felt the group would then give him, caused him to sweat even more. The patient found himself becoming more self-conscious of his sweating, and discovered it was progressively harder to engage in social situations where others might be watching him.

Nonetheless, the patient craved social contact. Over time, however, group therapy grew intolerable, and exposure therapy for his fear of queuing in cafeterias and grocery shops was unacceptable to him because of the physiological threat to his temperature and seizure control. He appears to have been socially conditioned to his phobia, which led to his social avoidance and fears of sweating attacks.

His social phobia is unusual, in that it began at a relatively late age in an otherwise normal individual, more clearly linking its development to a socially conditioned response to his pathological sweating. Pharmacological intervention had to be ruled out, as beta-blockers had not helped control his temperature in the past, and his present regimen of phenobarbitone and cyproheptadine was the only one of many interventions that had forestalled what had been a life-threatening condition.

Discussion

There are many organic causes of anxiety states (Goldberg, 1988). There are also unusual phobias that may be directly related to organic causes (Pratt & McKenzie, 1958; Marks, 1981). However, there has been little to link organic disorders to social phobia. In DSM-III-R (American Psychiatric Association, 1987), social phobia is defined as a persistent fear of one or more situations in which the person is exposed to possible scrutiny by others and fears that he or she may say something or act in a way that will be humiliating or embarrassing. Our patient avoided these situations not merely because they were embarrassing, but because this embarrassment further led to pathological sweating with potentially severe physiological repercussions. This fear of social situations fed on itself, as the patient would sweat more, become more embarrassed, sweat yet more, and then his temperature would drop so low that he sometimes felt he would not have the physical energy to escape the sweat-provoking situations.

Although this case is highly unusual, it does provoke consideration of some theoretical difficulties in defining phobias. First, there is the possibility that there are some people with intervening medical conditions for whom social phobias may in some broad sense be adaptive, that is, they will avoid situations where anxiety or embarrassment might cause considerable physiological difficulties. Originally, our patient did not have such a physiological response to social situations, but developed a phobia to them over a period of approximately one year. Before developing this social phobia, he could face similar social situations with equanimity.

Secondly, this case points up the difficulty of easily dismissing patients' claims that their avoidance of certain situations may be rationally justified by the overwhelming anxiety and strong emotion caused by their phobias and fears. There is now considerable evidence linking panic disorder and increased cardiovascular mortality (Coryell *et al*, 1982), and data that this may possibly be related to subgroups of patients with covert organic disorders are just beginning to appear (Kahn *et al*, 1987). Although the most frightening experience of a phobia may be the fear itself, the physiological sequelae of such fears may also be important. Thus, although phobias may begin as irrational fears, they may later exacerbate real physiological difficulties, that may, as in this case, provide 'rational' reasons to avoid experiences that might potentially cause physical harm.

References

American Psychiatric Association (1987) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn, revised) (DSM-III-R). Washington, DC: APA.

Coryell, W., Noyes, R. & Clancy J. (1982) Excess mortality in panic disorder. *Archives of General Psychiatry*, **37**, 701–703.

Goldberg, R. J. (1988) Anxiety in the medically ill. In *Principles of Medical Psychiatry* (eds A. Stoudemire & B. S. Fogel), pp. 177–204. New York: Grune & Stratton.

Kahn, J. P., Drusin, R. E. & Klein, D. F. (1987) Idiopathic cardiomyopathy and panic disorder: clinical association in cardiac transplantation. *American Journal of Psychiatry*, **144**, 1327–1330.

Johnson, M. H. & Jones, S. N. (1985) Status epilepticus, hypothermia and metabolic chaos in a man with agenesis of the corpus callosum. *Journal of Neurology, Neurosurgery and Psychiatry*, **48**, 480–483.

Marks, I. (1981) Space "phobia": a pseudo-agoraphobic syndrome: fear of absent visuospatial support (open spaces) and of falling. *Journal of Neurology, Neurosurgery and Psychiatry*, **44**, 387–391.

Noel, P., Hubert, J. P., Ectors, M., *et al* (1973) Agenesis of the corpus callosum associated with relapsing hypothermia. *Brain*, **96**, 359–368.

Pratt, R. T. & McKenzie, W. (1958) Anxiety states following vestibular disorders. *Lancet*, *ii*, 347–349.

Shapiro, W. R., Williams, G. H. & Plum, F. (1969) Spontaneous recurrent hypothermia accompanying agenesis of the corpus callosum. *Brain*, **92**, 423–436.

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A Family with Alzheimer's Disease

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A family with clinically diagnosed Alzheimer's disease in three siblings is described. The inheritance of Alzheimer's disease in this pedigree is consistent with autosomal dominant inheritance.

Historically, Alzheimer's disease has been divided into pre-senile and senile dementia of Alzheimer type (PDAT and SDAT respectively), depending upon whether the age at onset of the illness is before or after 65. While many investigators (e.g. Terry & Katzman, 1983) hold the view that the disease is essentially identical irrespective of the age at onset, this is by no means universally accepted, and Sourander & Sjogren (1970) believe that distinctions can be made. However, PDAT and SDAT may not be a unitary disorder, although the clinical features may be quite similar: neurohistological (Tagliavini & Pilleri, 1983) and neurochemical (Rossor *et al*, 1984) differences point towards a distinction between the two.

Various modes of transmission have been suggested, including multifactorial inheritance (Sulkava *et al*, 1979), regularly manifest autosomal dominant trait (Nee *et al*, 1983), autosomal dominant transmission with reduced penetrance (Constantinides *et al*, 1962), and polygenic inheritance (Whalley *et al*, 1982). Other investigators have reported discordance in identical twins (Renvoize *et al*, 1986) and environmental aetiological factors have been postulated.

This study is an investigation of a family with three siblings affected by Alzheimer's disease.

Case report

All three patients were referred for assessment to a consultant psychiatrist by their respective general practitioners between 1982 and 1985. Additional information was collected from family members and past medical records. Using the National Institute of Health (NIH) consensus criteria (McKhann *et al*, 1984), a clinical diagnosis of probable Alzheimer's disease was made in each case.

In all three cases, haemoglobin, full blood count, erythrocyte sedimentation rate, urea and electrolytes, liver function tests, blood glucose, serum folate, and vitamin B12, serological tests for syphilis and MSU were normal. JJ and WV (see below) also had normal thyroid function tests.

Family history

Their father (subject II-7, Fig. 1) had a long history of chronic confusion and tendency to wander. He was otherwise physically well until the time of his death at the age of 84 following a stroke. Their mother (subject II-6) died at the age of 72 from carcinoma of the oesophagus. Their maternal grandfather (subject I-2) and a maternal aunt (subject II-5) had been diagnosed as suffering from dementia. Neither had history of cardiovascular disease. A brother (subject III-2) died of a brain tumour at the age of 18 and two siblings (subjects III-7 and 8) died in their infancy. Two sisters (subjects III-5 and 6), aged 62 and 57, are alive and well.

JJ was a bachelor; WV has three children, and EH two; all are alive and well.

There is no history of movement disorder or any other neurological or cardiovascular illness in the family.

Case 1 (subject III-4)

EH, a 55-year-old housewife, presented with a two-year history of progressive forgetfulness, verbal aggression, and wandering tendencies, in 1980. In 1984, she was admitted to a psychogeriatric unit for assessment after her wandering on the streets without clothes and shouting obscenities at passers-by had caused considerable disruption and embarrassment in the local community. She was globally disorientated; all facets of her memory were grossly impaired, and she confabulated. Neurological examination showed nominal aphasia, receptive and expressive dysphasia, and dyspraxia. Physical examination showed no abnormality except for non-progressive, slightly increased tendon reflexes on the right side. Blood pressure was normal; arteriosclerotic changes were absent. Thyroid function tests revealed hypothyroidism with the serum chemistry as follows: T_4

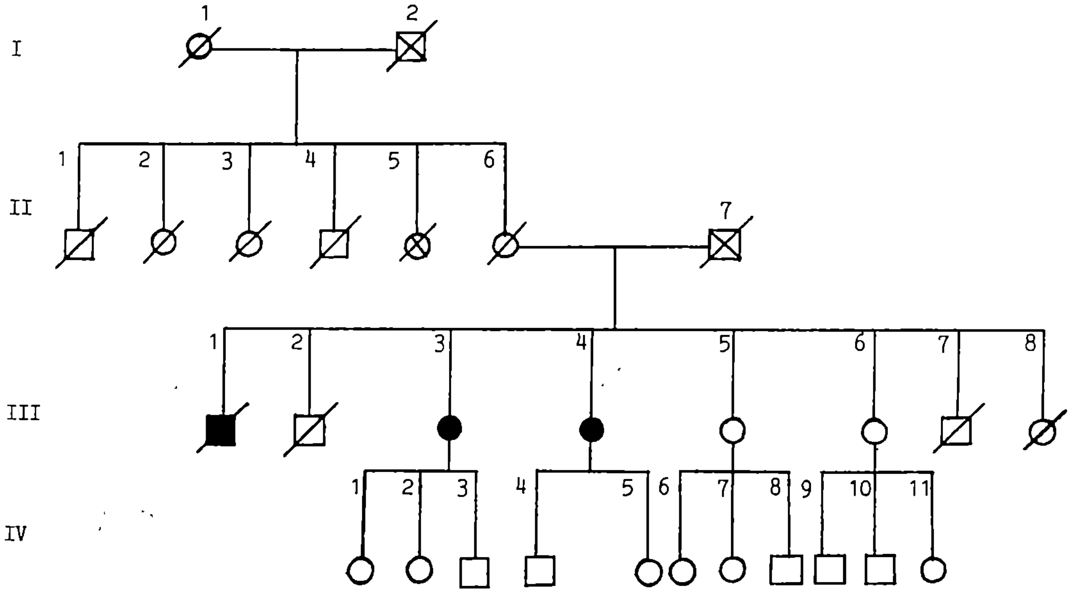

FIG. 1. Pedigree of the family with Alzheimer's disease. □ Male, ○ female, ■ Alzheimer's disease, ⊠ possible Alzheimer's disease, □ unaffected, ø deceased.

51 nmol/l (normal range 64–144 nmol/l), thyroid-stimulating hormone 46 mIU/l (normal range 0–8 mIU/l), and free-thyroxine index 49 (normal range 56–156). Correction of the deficiency made no difference to her mental state. EEG did not show any specific changes. Computerised tomography (CT) was reported as showing mild to moderate atrophy.

Over ten years she has continued to deteriorate both mentally and physically. She is incontinent of urine, unable to feed or dress herself, and requires considerable nursing input and supervision. She is presently an in-patient on a long-stay ward.

Case 2 (subject III-3)

In 1980, at the age of 59 years, WV started becoming forgetful, neglecting her domestic chores and repeatedly getting lost, even in the vicinity of her home. Over the next five years, her memory continued to disintegrate and she became increasingly dependent on her husband. During this period, she had several admissions to hospital, initially for assessment, and subsequently for respite care. As her mental state deteriorated, agitation gave way to aimless wandering, lack of personal hygiene to faecal smearing, nominal aphasia, receptive and expressive dysphasia to meaningless utterances, and variable orientation to confabulation and total confusion. She became emotionally labile and showed both constructional and dressing dyspraxias. Her performance on Isaac's Set Test for cerebral failure (Isaacs & Akhtar, 1972) dropped from 14/40 to 0/40. Physical examination revealed bilateral pin-rolling tremor and slightly increased tone in the extremities. Otherwise, systemic examination, including cardiovascular system, was normal.

Since 1985, she has been an in-patient on a long-stay ward for highly dependent patients, where deterioration in her mental and physical condition has continued.

Case 3 (subject III-1)

JJ's illness was of insidious onset. In 1980, at the age of 62 years, he started misplacing house keys, leaving the cooker on, and wandering. Over the next seven years there was a gradual decline in his memory, intellect, and personality. Formal cognitive assessment in 1984 using Clifton Assessment Procedures for the Elderly (Pattie & Gilleard, 1975), showed his overall score to be 9 (grade D), indicating a marked degree of intellectual impairment and dependency. Serial testing using Isaac's Set Test for cerebral failure showed a gradual drop in his performance over one year. In 1985, he was admitted to a psychogeriatric assessment unit. He was disorientated in time, place, and person; remote and recent memory and immediate recall were all markedly impaired, and his concentration was very poor. Testing of his higher functions revealed nominal, receptive and expressive dysphasias, and constructional and dressing dyspraxias. Physical examination was unremarkable; there was no evidence of arteriosclerosis, and his blood pressure was normal. Deterioration in his physical and mental condition continued. He became emaciated, doubly incontinent, incomprehensible, and developed myoclonic seizures. About seven years after the onset of his illness and six weeks after sustaining a fracture of his femur, he died of bronchopneumonia.

Discussion

Breitner & Folstein (1984) have described a distinct clinical entity called 'familial Alzheimer's disease', identified by language disorder and apraxia. These features were prominent very early on in all three cases described above.

EH's thyroid dysfunction is of interest, as an increased incidence of thyroid disease in the past history of affected women has been reported (Heyman *et al*, 1983). A familial association has also been made between increased infant mortality and Alzheimer's disease (Heston *et al*, 1981). In the family described above, there were two deaths in infancy, although the cause of death in both cases is unknown.

Another interesting finding was the relationship between birth order and age at onset of Alzheimer's disease. In the above family, the age at onset of the illness was inversely related to birth order: the lower the position in the birth order, the younger the age at onset of the illness. Although no firm conclusions can be drawn from a study of a single family, this is in contrast to Whalley *et al* (1982) who did not find any 'position effect'.

Heston *et al* (1981) have reported a familial association between Alzheimer's disease, Down's syndrome and immunoproliferative disorders, although no such cases were found in this family.

The maternal age at the birth of the youngest affected child (EH) was 25 years. Cohen *et al* (1982) have reported a significantly increased mean maternal age at the time of birth of DAT patients when compared with age-matched controls, while Knesevich *et al* (1982) could not find any statistical difference.

Renvoize *et al* (1986) have emphasised the role of environmental factors in the aetiology of Alzheimer's disease but, because retrospective study of the environmental conditions to which these three subjects were exposed can be inexact and subjective, I have made no such attempt.

The pattern of transmission in this pedigree of familial Alzheimer's disease would appear to be autosomal dominant inheritance with incomplete penetrance, as subject II-6 was unaffected on the maternal side of the pedigree. In the absence of any informants, it was not possible to obtain the family record of subject II-7, and thereby follow the paternal pedigree.

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References

Breitner, J. C. S. & Folstein, M. F. (1984) Familial Alzheimer dementia: a prevalent disorder with specific clinical features. *Psychological Medicine*, 14, 63–80.

Cohen, D., Eisdorfer, C. & Leverenz, J. (1982) Alzheimer's disease and maternal age. *Journal of the American Geriatric Society*, 30, 656–659.

Constantinidis, J., Garrone, G. & Ajuriaguerra, J. (1962) L'heredite des demences de l'age avance. *Encephale*, 51, 301–344.

Heston, L. L., Mastri, A. R., Anderson, E., *et al* (1981) Dementia of the Alzheimer type. Clinical genetics, natural history and associated conditions. *Archives of General Psychiatry*, 38, 1085–1090.

Heyman, A., Wilkinson, W. E., Hurwitz, B. J., *et al* (1983) Alzheimer's disease: genetic aspects and associated clinical disorders. *Annals of Neurology*, 14, 507–515.

Isaacs, B. & Akhtar, A. J. (1972) The set test: a rapid test of mental function in old people. *Age and Aging*, 1, 222–226.

Knesevich, J. W., LaBarge, E., Martin, R. L., *et al* (1982) Birth order and maternal age effect in dementia of the Alzheimer type. *Psychiatry Research*, 7, 345–350.

McKhann, G., Drachman, D., Folstein, M., *et al* (1984) Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA work group under the auspices of the Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology*, 34, 939–944.

Nee, L. E., Polinsky, R. J., Eldridge, R., *et al* (1983) A family with histologically confirmed Alzheimer's disease. *Archives of Neurology*, 40, 203–208.

Pattie, A. H. & Gilleard, C. J. (1979) *Manual of the Clifton Assessment Procedures for the Elderly (CAPE)*. Sevenoaks: Hodder & Stoughton.

Pearce, J. & Miller, E. (1973) *Clinical Aspects of Dementia*. London: Baillière Tindall.

Renvoize, E. B., Mindham, R. H. S., Stewart, M., *et al* (1986) Identical twins discordant for presenile dementia of Alzheimer type. *British Journal of Psychiatry*, 149, 509–512.

Rossor, M. N., Iverson, L. L., Reynold, G. P., *et al* (1984) Neurochemical characteristics of early and late onset types of Alzheimer's disease. *British Medical Journal*, 228, 961–964.

Sourander, P. & Sjogren, H. (1970) The concept of Alzheimer's disease and its clinical implications. In *Alzheimer's Disease*, Ciba Foundation Symposium (eds Wolstenholme, G. E. W. & O'Connor, M.). London: Churchill.

Sulkava, R., Rossi, L. & Knuutila, S. (1979) No elevated sister chromatid exchange in Alzheimer's disease. *Acta Neurologica Scandinavica*, 59, 156–159.

Tagliavini, F. & Pilleri, G. (1983) Neuronal counts in basal nucleus of Meynert in Alzheimer's disease and in simple senile dementia. *Lancet*, *i*, 469–470.

Terry, R. D. & Katzman, R. (1983) Senile dementia of the Alzheimer type. *Annals of Neurology*, 14, 497–506.

Whalley, L. J., Carothers, A. D., Collyer, S., *et al* (1982) A study of familial factors in Alzheimer's disease. *British Journal of Psychiatry*, 140, 249–256.

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Pericentric Inversion Chromosome 9 and Personality Disorder

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A case of pericentric inversion chromosome 9 with an associated personality disorder is reported. There is justification for a more widespread cytogenetic screening of psychiatric disorders of this type.

Most foetuses with chromosomal abnormality do not survive. Abnormalities involving chromosomes 5p, 13, 18, and 21 are well recognised. There are many cases of mental and physical handicap involving unbalanced chromosomal rearrangements of chromosome 9 (Schinzel, 1984). We report a case of pericentric inversion chromosome 9 associated with personality disorder.

Case report

A 21-year-old single man was admitted in an excitable state, following a series of bogus telephone calls to various emergency services.

The patient was born to non-consanguinous parents who are functioning at an average level of intelligence. The first-born child in the family died at the age of one week; the patient was born six years later. There was no history of excessive consumption of alcohol by his mother during pregnancy. The delivery and milestones were normal, but at the age of ten, he was seen by a psychiatrist with complaints of "fussiness, excessive washing, and of being very religious". He also had trouble with the police after breaking a window of a parked car. He was found to be a pleasant, cooperative boy who was left handed. His eyes were sloping down laterally, his head circumference was 56.5 cm (above the 97th percentile), his height was 1.42 m and his weight was 32.7 kg (both between the 50th and 75th percentiles). All tendon reflexes were brisk, and the rest of his physical examination was normal. His IQ on the Wechsler Intelligence Scale for Children was 82, with non-significant difference between verbal and performance subscales.

He was subsequently admitted to various psychiatric hospitals on different occasions with behavioural problems, during which hysterical, immature, and psychopathic personality disorders were considered as diagnoses. As he grew up, he acquired a few homosexual contacts.

The patient's present mental state examination showed him to be shy, immature, and demanding, with limited insight into his condition. He was anxious and emotionally unstable, and experienced a good deal of difficulty in social situations. He tended to be naïve and unrealistic in his dealings with others. His appearance was normal except for laterally sloping eyes with narrow palpebral fissures. His systemic and neurological examinations were normal. His investigations were normal, except the computerised tomography brain scan showed a minor degree of frontal lobe atrophy. On psychological assessment his functioning fell within low average range, with a total score of 80 on the Wechsler Adult Intelligence Scale; he experienced greatest cognitive deficit in the areas of immediate memory, attention, concentration, and response speed.

Cytogenetic findings

Chromosome preparations from a short-term lymphocyte culture were analysed using GTG and CBG banding techniques. The patient was shown to have a pericentric inversion of a number 9 chromosome (Fig. 1). An inversion is a reversal of a chromosome segment, and originates when two breaks occur within a chromosome and the broken fragment is rotated 180° and reinserted into the gap (Fig. 1c). Since no chromosomal material is lost or gained, this may be thought of as a balanced rearrangement. The breakpoints p13 and q13 were the probable breakpoints in this case.

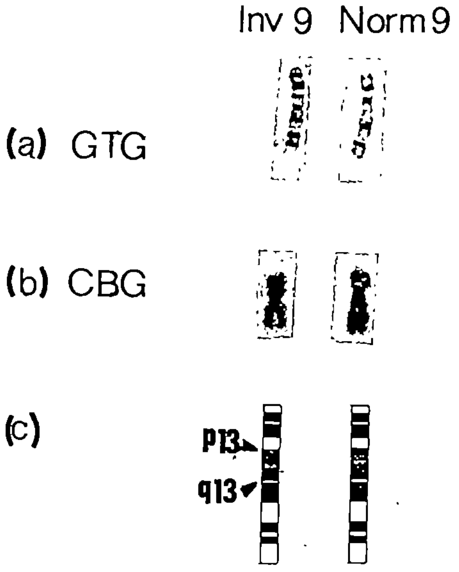

FIG. 1. The inverted chromosome 9 and its normal homologue: (a) G bands by trypsin using Giemsa. (b) Centromeric banding – note the subcentromeric dark band appears in the short arm in the inverted chromosome. (c) Diagrammatic representation (International System for Human Cytogenetic Nomenclature, 1985): the inverted segment is between p13 and q13.

The main cytogenetic problem associated with inversions are at a meiotic level, with the possible resulting formation of gamates with duplicated or deficient chromosome material. The pericentric inversion described here was also found in the patient's mother, who showed no physical or psychiatric abnormality. The patient's karyotype is 46,XY,inv.(9)(p13q13).

Discussion

Pericentric inversion chromosome 9 is the most common pericentric inversion in the human karotype (Kaiser, 1984). In our case, this pericentric inversion was observed in both the patient and his mother. It has been reported that carriers of apparently balanced rearrangements have shown serious phenotypic defects while their parental chromosomes with the same balanced rearrangement were associated with normal phenotypes (Jacobs, 1974). Should a chromosomal or genetic reason be responsible for the personality disorder in the patient, it may be due to gene mutation at or near the breakpoints in the affected person. Since a pericentric inversion is an intrastructural rearrangement, there may be a genetic reason for the patient's condition.

A search of the literature showed a prevalence range for pericentric inversion of 0.26–3.5% in amniotic fluid specimens (Hsu *et al*, 1987), and this inversion was found in 3% of couples in which the women were ascertained to have two or more spontaneous abortions (Campana *et al*, 1986). Similarly, Kiss & Osztovics (1981) found this aberration in 1.9% of dysmorphic children under one year of age, and they stated that this phenomenon, earlier regarded as a polymorphism or normal variant, seems to be playing an imported role in the aetiology of unspecified dysmorphic syndromes. Most strikingly, a Japanese study (Kodama, 1982) showed that the prevalence of pericentric inversion chromosome 9 in institutionalised patients was 4.2 times higher than that in the general population. One study reported the association of pericentric inversion chromosome 9 in 15.7% of male homosexuals (Manolov *et al*, 1985).

Our case uniquely represents the association of personality disorder and pericentric inversion chromosome 9. As this aberration is not uncommon, chromosome studies of psychiatric patients with personality disorder may show such association in a greater number of subjects. Although our patient has acquired a few homosexual contacts, we are not certain whether this is due to his personality disorder or directly associated with the pericentric inversion.

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References

Campana, M., Serra, A. & Neri, G. (1986) Role of chromosome aberrations in recurrent abortions: a study of 269 balanced translocations. *American Journal of Medical Genetics*, 24, 341–356.

Hsu, L. Y., Benn, P. A., Tannenbaum, H. L., *et al* (1987) Chromosomal polymorphisms of 1, 9, 16 and Y in 4 major ethnic groups: a large prenatal study. *American Journal of Medical Genetics*, 26, 95–101.

International System for Human Cytogenetic Nomenclature (1985) *Report of the Standing Committee on Human Cytogenetic Nomenclature* (ed. K. S. Karger). Basel: ISCN.

Jacobs, P. A. (1974) Correlation between euploid structural chromosome rearrangements and mental subnormality in humans. *Nature*, 249, 164–165.

Kaiser, P. (1984) Pericentric inversions. Problems and significance for clinical genetics. *Human Genetics*, 68, 1–47.

Kiss, P. & Osztovics, M. (1981) Cytogenetic investigations in 817 dysmorphic babies. *Zeitschrift für die Gesamte innere Medizin und ihre Grenzgebiete*, 36, 356–360.

Kodama, Y. (1982) Cytogenetic and dermatoglyphic studies on severely handicapped patients in an institution. *Acta Medica Okayama*, 36, 383–397.

Manolov, G., Manolova, Y., Sonnabend, J., *et al* (1985) Chromosome aberrations in peripheral lymphocytes of male homosexuals. *Cancer Genetics and Cytogenetics*, 18, 337–350.

Schinzel, A. (1984) Chromosome 9. In *Catalogue of Unbalanced Chromosome Aberrations in Man*, pp 350–394. Berlin: Walter de Gruyter.

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Psychiatric Features of Adult GM2 Gangliosidosis

J. STREIFLER, M. GOLOMB and N. GADOTH

The report describes three unrelated Ashkenazi Jewish women with adult GM_2 gangliosidosis in whom mental symptoms were prominent, mimicking different psychiatric disorders, and thus delaying accurate diagnosis.

The nature of the neurological impairment due to neuronal storage diseases is influenced by the age of onset. When appearing early in life, intellectual deterioration is the main clinical feature, while when manifested late in life, spasticity and Babinski signs may herald the disease, and intellectual deterioration can appear later (Freeman & McKhann, 1969). In a number of neuronal storage diseases of juvenile and adult onset, psychiatric manifestations may be the presenting signs and, as such, may delay the correct diagnosis (Adams & Victor, 1985). Disorders such as Wilson's disease, Kufs' ceroid lipofuscinosis, and metachromatic leucodystrophy are a few examples.

The infantile Tay–Sachs disease was considered the only form of GM$_2$ gangliosidosis until two decades ago. However, it became apparent that there are other forms of GM$_2$ gangliosidosis due to other genotypic forms of deficiency in the enzyme hexosaminidase A (Hex A) (Rapin *et al*, 1976).

The adult form of GM$_2$ gangliosidosis (AGG) is an autosomal recessive inherited neuronal storage disease with predilection to Ashkenazi Jews similar to the infantile form (Argov & Navon, 1984). AGG is characterised by clinical syndromes expressed as spinocerebellar degeneration, motor neuron disease, dementia, involuntary movements, and stuttering (Johnson, 1981). Only in the last few years, after reviewing a significant number of cases, has it become evident that psychiatric impairment is an essential part of the disease in about 30% of the patients, manifested usually as recurrent hebephrenic-like psychotic attacks or as depression (Argov & Navon, 1984; Navon *et al*, 1986). The diagnosis is easily confirmed by demonstrating a deficiency of Hex A activity in the serum, leucocytes, and skin fibroblasts (Navon *et al*, 1973).

As a considerable number of patients may present with psychiatric manifestations mimicking primary psychiatric disorders, it seems worthwhile to outline the various psychiatric aspects of this disease, and to illuminate this rare entity in the psychiatric literature. The present report describes three typical patients with AGG in whom the psychiatric illness posed the main problem.

Case reports

A 38-year-old woman of Ashkenazi Jewish extraction was referred to the Department of Neurology from a psychiatric hospital because of the onset of grand mal seizures. The family and early personal histories were unremarkable.

Psychiatric manifestations began at the age of 16 with a gradual change in character. She became aggressive and difficult to control, and suffered from social and environmental maladjustment. Subsequently muffled speech and a decline in school performance were noticed.

At the age of 17 she became acutely agitated, disorientated, and experienced sexual paranoid delusions. She was then admitted to a psychiatric ward, believed to be suffering hebephrenic schizophrenia, and was treated accordingly.

During the following four years she had seven more hospital admissions for acute psychotic episodes. Response to drug therapy was unpredictable, but usually unsatisfactory. Sometimes improvement was noted after withdrawal of treatment. In between these attacks a decline in personality was observed. Physical rehabilitation attempts were unsuccessful partly because of her clumsiness with her hands. A few years later, bouts of involuntary movements and postural instability appeared, and were interpreted as tardive dyskinesia. At the age of 31, she was referred for chronic hospitalisation because of severe restriction of personality and bouts of agitation.

During the present admission, neurological examination disclosed dysarthria, ataxia hypotonia, and impaired cerebellar functions. Involuntary movements of the face, mouth, tongue, and limbs along with severe psychomotor slowness were present. Computerised tomography (CT) of her brain was compatible with cerebellar degeneration. Hex A activity was deficient in the serum, leucocytes, and skin fibroblast, and was in the heterozygote range in several other members of the family. The biochemical data were compatible with autosomal recessive inheritance of the enzymatic defect.

Case 2

A 44-year-old married woman of Jewish Ashkenazi extraction, mother of three healthy children, was referred to the Department of Neurology from a psychiatric hospital for evaluation of frequent falls. The family history and the history of early psychomotor development were unremarkable.

At the age of 42, she suffered from an episode of depressed mood with loss of appetite, sleep disturbance, lack of interest, and suicidal thoughts. This episode lasted for about a month, during which she lost 15 kg. Disturbances in menstruation were noted at that time, and involutional depression was diagnosed.

For the following two years she was under psychiatric out-patient care for recurrent depressive episodes. Her first admission to a psychiatric hospital was initiated by the appearance of paranoid delusions and auditory hallucinations. During this admission, frequent falls were noted. A neurological evaluation revealed impaired cerebellar functions with marked truncal ataxia. Her speech was explosive and dysarthric, and there were involuntary movements of the lips and tongue. Proximal weakness of the legs with diminished tendon jerks were found. Upper limb reflexes were hyperactive. Brain CT indicated cerebellar degeneration. Hex A activity was deficient in the serum, leucocyte, and skin fibroblast, and was in the heterozygote range in several members of the family, compatible with autosomal recessive inheritance of the biochemical defect.

During the following year, she suffered a second psychotic episode, and a year later she entered a prolonged

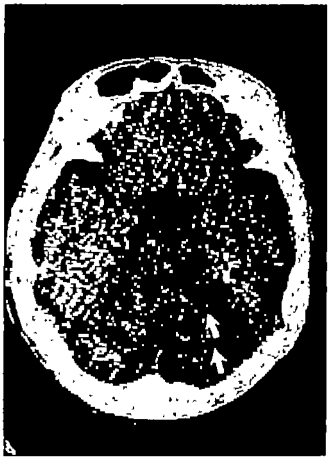

FIG. 1. Cerebral CT from case 1 shows distinct prominence of cerebellar folia (arrows) indicative of cerebellar atrophy.

depressive state. Since then, there have been several admissions for depressive episodes. Manic episodes were not observed during the follow-up period, and the psychiatric picture was of major depression. Antidepressive drugs were not used as they were considered to be contraindicated.

Case 3

A 24-year-old woman of Jewish Ashkenazi extraction was evaluated for walking instability and frequent falls. Her early history was unremarkable, but during secondary school she underwent psychological treatment for 'stuttering', and during her army service (age 19–20) she noticed difficulty in climbing stairs and completing hikes, mainly because of frequent falls. After her army service she could not keep a permanent job because of clumsiness and immature speech and behaviour.

At the age of 23, during the spring, she suffered a depressive episode with paranoid delusions related to her employers. This remitted after a month.

As her motor performance deteriorated, she underwent neurological evaluation. She had an expressionless face, with a peculiar stare, and a dysarthric speech, a waddling gait with proximal weakness of both legs, her tendon reflexes were symmetrically brisk and hyperactive, and bilateral Babinski sign was elicited. Brain CT was compatible with cerebellar degeneration. During the following two years in each spring, the patient suffered recurrent depressive episodes. Between the attacks, personality regression was noted, with childish behaviour and concrete thinking. During the third episode a full-blown paranoid psychosis emerged, which was marked by impaired consciousness, memory disturbances, and vivid visual hallucinations of small animals such as snakes and cockroaches.

Drug therapy with antipsychotic drugs (haloperidol and perphenazine) resulted in severe adverse reactions, mainly of extrapyramidal type. The patient developed a catatonic-like state which disappeared only after medications were stopped. This psychotic episode lasted over six months.

In her family a younger brother suffers from a similar neurological disability (stuttering and frequent falls). Hex A activity was deficient in serum leucocytes and skin fibroblasts of the patient and her brother.

Discussion

The three cases described present a variety of neuropsychiatric features. The similar neurological abnormalities comprise a clinical picture consisting of spinocerebellar syndrome, lower motor neuron disease, dementia, and involuntary movements with CT demonstration of cerebellar degeneration (Fig. 1).

The biochemical diagnosis confirmed that this clinical condition is inherited as an autosomal recessive trait: homozygotes and heterozygotes were detected in each of the three families (Table I).

In contrast to the almost uniform neurological impairment, the psychiatric manifestations were different in each patient.

In case 1 an almost 'typical' picture of disorganised (hebephrenic) schizophrenia was present. This diagnosis is based on the following: onset at adolescence, disorganised thinking, delusions and auditory hallucinations, accompanied by emotional disturbances, inappropriate affect, and marked regression. The clinical course is characterised by recurrent psychotic attacks leading to gradual decline in personality and subsequently to chronic in-patient care.

The second patient developed an episode of depression which was diagnosed as involutional depression. Two years later she suffered two episodes of paranoid psychotic attacks and later developed a typical picture of major depression. This is a case of recurrent psychotic depression.

The third patient suffered from recurrent depressive episodes, with paranoid delusions and prominent organic elements. Her short period of delirium and the hallucinations of small animals resembles the clinical picture of delirium tremens or alcoholic hallucinosis. This picture has not been previously described in AGG.

All three patients, as a rule, responded poorly to conventional psychiatric drug therapy. The third patient's response was unusual, as she developed severe adverse effects to commonly used antipsychotic drugs. The poor response to drug therapy may be explained in part by the fact that *in-vitro* tricyclics may have a depressive effect on the activity of Hex A, and it has been shown that lipidoses can be induced by tricyclics and phenothiazine drugs (Navon *et al*, 1986).

TABLE I
Hex A activity: % heat-labile activity

	Serum	*Leucocytes*	*Skin*	*Genotype*
Patient 1	0	5.2	0	Homozygote
Father	39.9	46.1	27.5	Heterozygote
Mother	ND	50.3	36	Heterozygote
Brother	68.4	58.8	ND	Normal
Patient 2	0	9	9.5	Homozygote
Father	41	ND	32	Heterozygote
Mother	32.2	48	26	Heterozygote
Brother	44	52	ND	Heterozygote
Patient 3	1.4	7.4	3.6	Homozygote
Brother	3.3	11.8	21.5	Homozygote
Normal values[1]	48–64	58–69	50–68	
Heterozygote range	32–46	37–54	20–27	
Homozygote range	0–13	0–13	1–12	

1. Navon *et al* (1973).
ND – not determined.

A variety of psychiatric manifestations is known in other organic diseases, such as systemic lupus erythematosus, Beçhet's disease, lues, and Wilson's disease. Diagnostic errors were made in those diseases also.

It is recommended, therefore, that in psychotic patients, especially of Ashkenazi Jewish origin, suffering from involuntary movements and showing poor response to commonly used anti-psychotic drugs, the possibility of AGG should be considered and appropriately evaluated.

References

ADAMS, R. D. & VICTOR, M. (1985) The inherited metabolic diseases of the nervous system. In *Principles of Neurology*, pp. 753–754. New York: McGraw-Hill Book Company.

ARGOV, Z. & NAVON, R. (1984) Clinical and genetic variations in the syndrome of adult GM$_2$ gangliosidosis, resulting from hexosadminidase A deficiency. *Annals of Neurology*, **16**, 14–20.

FREEMAN, J. M. & MCKHANN, G. M. (1969) Degenerative diseases of central nervous system. *Advances of Pediatrics*, **16**, 121–175.

JOHNSON, W. G. (1981) The clinical spectrum of hexosaminidase deficiency diseases. *Neurology*, **31**, 1453–1456.

NAVON, R., PADEH, B. & ADAM, A. (1973) Apparent deficiency of hexosaminidase A in healthy members of a family with Tay Sachs disease. *American Journal of Human Genetics*, **25**, 287–293.

——, ARGOV, Z. & FRISCH, A. (1986) Hexosaminidase A deficiency in adults. *American Journal of Medical Genetics*, **24**, 179–196.

RAPIN, I., SUZUKI, K., SUZUKI, K., *et al* (1976) Adult (chronic) GM$_2$ gangliosidosis. *Archives of Neurology*, **33**, 120–129.

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Adverse Interaction Between Cimetidine and Chlorpromazine in Two Cases of Chronic Schizophrenia

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The treatment of two chlorpromazine-medicated chronic schizophrenics with cimetidine resulted in excessive sedation, which necessitated a reduction in chlorpromazine dosage. Eventual discontinuation of cimetidine therapy led to a return of schizophrenic symptoms, which responded to an increase in chlorpromazine dosage to previous levels.

Howes *et al* (1983) reported that the chronic administration of cimetidine produces a fall in the steady-state plasma concentrations of chlorpromazine. We present the case histories of two chronic schizophrenics seen in our hospital during July and August of 1987, which do not support this finding.

Case reports

Case 1

Ms VT, a 53-year-old lady with mild mental handicap, a resident of a long-stay ward, was maintained on chlorpromazine (100 mg q.i.d.). A clinical diagnosis of reflux oesophagitis was made, and confirmed at gastroscopy. She was commenced on cimetidine (400 mg b.i.d.) and her dyspeptic symptoms were relieved. After seven days, she became progressively more sedated, spending more and more time in bed, with no recurrence of her schizophrenic symptoms. Her chlorpromazine dosage was reduced to 50 mg q.i.d., dramatically increasing her alertness, mobility, and motivation.

Cimetidine therapy was withdrawn after eight weeks, and the patient became loud and agitated, with delusions of persecution. Chlorpromazine dosage was increased to 100 mg q.i.d. and her symptoms resolved.

Case 2

Mr JD, a 47-year-old man in our high-support hostel, was maintained on chlorpromazine (100 mg t.d.s.). He developed anorexia, abdominal pain, and profound weight loss over a fortnight. A diagnosis of peptic ulcer was confirmed at endoscopy, and cimetidine (400 mg b.i.d.) was commenced. After about five days he became drowsy and lethargic, and took to bed. Following a reduction of his chlorpromazine dosage to 50 mg t.i.d. he became alert and active, and returned to his normal routine. Discontinuation of his cimetidine therapy was followed by a deterioration in his mental state. The latter improved markedly when his chlorpromazine dosage was doubled.

Discussion

We describe, for the first time, two cases of an adverse interaction between cimetidine and chlorpromazine. Our suggestion is that this interaction causes a reduction in the metabolism of chlorpromazine, with resultant sedation and deterioration in performance levels (McMillan *et al*, 1978).

The main pathways involved in the breakdown of chlorpromazine are oxidation and conjugation mechanisms (Baldessarini, 1980), and it is in the oxidative mechanism that cimetidine is most likely to exert its effect. The findings of Feely & Wormsley (1983) suggest that cimetidine binds to the cytochrome P450 oxidising system in hepatic microsomes, and so reduces the metabolism of the many drugs which are eliminated by this oxidative pathway. The delayed clearances of diazepam (Klotz & Ruman, 1980) and oral anticoagulants (Flind, 1978) have been noted when cimetidine is administered concurrently, and it is our belief that chlorpromazine suffers a similar fate.

Chlorpromazine was originally introduced to potentiate the effects of cerebral depressants. It has also been noted to potentiate the actions of tricyclic antidepressants, and this too is felt to involve reduced hepatic metabolism (Baldessarini, 1980). It is interesting therefore, that cimetidine appears to potentiate the effects of chlorpromazine by its actions on hepatic microsomal enzymes. These effects on hepatic function have been noted before (e.g. Feely & Wormsley, 1983), and we feel that the pronounced sedative effects in our patients are due to the impaired clearance of chlorpromazine.

An alternative explanation for this adverse reaction would be that cimetidine produces sedative effects of its own, which are added to those of chlorpromazine. However, no antipsychotic activity has been attributed to cimetidine, despite its ability to cross the blood–brain barrier and produce both confusional and hallucinatory phenomena (Barnhart & Bowden, 1979). Such confusional states are usually seen in seriously ill patients who have impaired creatinine clearance (McMillan *et al*, 1978; Barnhart & Bowden, 1979). Cimetidine itself has been implicated in the impairing of renal function (McElligott, 1978), but there was no evidence of renal impairment in either of our patients. Cimetidine has also been cited as a cause of stupor (Jefferson, 1979) and of reversible anxiety state (Johnson, 1979), but such reports are anecdotal.

Our two cases show how an interaction between two commonly used drugs produces excessive sedation which remits upon reduction of chlorpromazine dosage. The binding of cimetidine to cytochrome P450 is felt to cause the problem, and as this mechanism is involved in the metabolism of haloperidol and other neuroleptics, a similar situation could arise in their use.

We suggest, therefore, that ranitidine might be a more appropriate anti-ulcer therapy for chronic schizophrenics, as it is not associated with alterations in the hepatic metabolism of other drugs. Our cases serve to warn clinicians of the possible complications of ulcer therapy for chronic schizophrenics stabilised on chlorpromazine.

References

BALDESSARINI, R. J. (1980) Drugs and the treatment of psychiatric disorders. In *The Pharmacological Basis of Therapeutics* (eds A. Goodman & L. S. Gillman), pp. 403–405. New York: MacMillan Publishing Co.

Barnhart, C. C. & Bowden, C. L. (1979) Toxic psychosis with cimetidine. *American Journal of Psychiatry*, **136**, 725–726.

Feely, J. & Wormsley, K. G. (1983) H_2 receptor antagonists – cimetidine and ranitidine. *British Medical Journal*, **286**, 695–697.

Flind, A. C. (1978) Cimetidine and oral anti-coagulants. *British Medical Journal*, *ii*, 1367.

Howes, C. A., Pullar, T., Sourindhrin, I., *et al* (1983) Reduced steady-state concentrations of chlorpromazine and indomethacin in patients receiving cimetidine. *European Journal of Clinical Pharmacology*, **24**, 99–102.

Jefferson, J. N. (1979) Central nervous system toxicity to cimetidine (abstract). *American Journal of Psychiatry*, **136**, 346.

Johnson, J. (1979) Cimetidine and psychiatric complications. *British Journal of Psychiatry*, **134**, 315–316.

Klotz, U. & Ruman, I. (1980) Delayed clearance of diazepam due to cimetidine. *New England Journal of Medicine*, **302**, 1012–1014.

McElligott, M. (1978) Impaired creatinine clearance after cimetidine. *Lancet*, *i*, 99.

McMillan, M. A., Ambis, D. & Sugal, J. H. (1978) Cimetidine and mental confusion. *New England Journal of Medicine*, **298**, 284–288.

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Mianserin-Induced Restless Legs Syndrome

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Restless legs syndrome was observed in three patients receiving mianserin. The symptoms resolved when the treatment was discontinued or reduced.

Mianserin, a tetracyclic piperazino-azepine compound, is a second-generation antidepressant that has attracted much attention since its introduction to clinical practice in 1975. In pre-clinical *in-vitro* studies, mianserin has been characterised as a moderate antagonist of pre-synaptic α_2-receptors, and as a poor blocker of serotonin uptake, without noticeable effect on acetylcholine receptors (Goodlet *et al*, 1977). Its overall efficacy is reported to be similar to that of conventional tricyclic antidepressants (Zis & Goodwin, 1979). Although mianserin lacks adverse cardiovascular effects and is distinguished by a lack of anticholinergic side-effects, it can cause several troublesome adverse effects: drowsiness, blood dyscrasias, arthralgia, oedema, and hypotension. However, we have not found any reports of mianserin-induced restless legs syndrome in the literature.

The restless legs syndrome (similar to neuroleptic-induced akathisia, which patients experience on lying down and attempting to fall asleep) is characterised by an unpleasant creeping sensation that affects primarily the legs, appears only at rest, and induces an irresistible urge to keep the limbs in motion (Montplaisir *et al*, 1985). We present what we believe to be the first three cases of mianserin-induced restless legs syndrome.

Case reports

Case 1

Mrs A, a 44-year-old married woman, met DSM-III criteria (American Psychiatric Association, 1980) for major depressive episode (dysphoric mood, slow speech, suicidal ideation, poor appetite, loss of energy, and insomnia). Physical examination and routine laboratory tests were normal. Mental status examination on admission revealed both depressed mood and affect. The patient started a regimen of 30 mg/day of mianserin, the dose increasing to 90 mg/day over one week. She became less suicidal and showed a definite improvement in mood and sleep.

After ten days of treatment with mianserin, Mrs A began to complain of difficulty in falling asleep, as she had poorly localised, non-throbbing aches in her lower legs. She was frequently found to move or rub her legs at rest, and she reported that she had to get up and walk around to obtain relief. The aches that characteristically began in the evenings also fragmented her sleep, during which the ward nurses observed repetitive leg movements. On day 12, we added 10 mg/day of diazepam in divided doses along with a hot-pack, but this did not alleviate her symptoms. On the following day a neurological examination proved unremarkable. Tests showed that she was not pregnant. Serum iron level was within the normal range. No uraemic or diabetic signs were observed. Mianserin was discontinued for three days, and the unpleasant sensation disappeared.

On day 16, we noted the re-emergence of psychomotor retardation and vegetative signs of depression. Mianserin was resumed and increased to 90 mg/day over four days, when the patient reported the recurrence of the unpleasant sensations in her legs, especially when she was trying to fall asleep. At this point, we suspected mianserin-induced restless legs syndrome, as there was no family history of restless legs syndrome. Mianserin was discontinued and gradually replaced by 100 mg/day amitriptyline. The syndrome again remitted and never reappeared. After 36 days of treatment, she was discharged on a maintenance dose of amitriptyline.

Case 2

Mrs B, a 49-year-old menopausal woman, was admitted to the hospital because of an insidiously progressive depression that had lasted for five months. On admission she was severely depressed, had lost 8 kg in weight, and suffered from anxiety and insomnia. She met DSM–III criteria for major depressive episode. There was no evidence of medical or neurological illnesses. She was given mianserin, at dose of 30 mg/day, increasing to 60 mg/day over seven days. Her depression somewhat improved.

On day 8 of treatment, she reported a disturbing feeling in her lower legs, chiefly in the evening, urging her to move her legs. She said that to obtain relief, she had to rub her legs vigorously. On the following day, she also complained of difficulty in falling asleep because of the symptom. She said she had to writhe in order to fall asleep. It was noticed that she was frequently awakened by involuntary jerks of the legs. The results of a neurological examination and comprehensive laboratory tests were unremarkable. There was no evidence of iron-deficiency anaemia, and uraemia, or diabetes. There was no family history of restless legs syndrome. When we discontinued mianserin and switched to amitriptyline, the symptoms of restless legs syndrome completely disappeared within three days. While she took a maintenance dose of amitriptyline (10 mg/day) the disturbing sensation never recurred.

Case 3

Mrs C was a 45-year-old married woman who was admitted with a three-week history of depressive symptoms characterised by depressed mood, loss of appetite, psychomotor agitation, insomnia, and sense of hopelessness. Her depression developed three months after she underwent a total hysterectomy for a uterine myoma. She met DSM–III criteria for major depressive episode. The results of medical, gynaecological, and neurological examinations were within normal range. We started treatment with 30 mg/day of mianserin and increased the dose to 90 mg/day over one week.

After two weeks of treatment she experienced an unpleasant sensation in her legs at night and complained of difficulty in falling asleep. She reported that rubbing or moving her legs vigorously brought only temporary relief. On neurological and medical examinations, there were no abnormalities, and she did not suffer from iron-deficiency anaemia, uraemia, or diabetes. There was no family history of restless legs syndrome. Drug-induced restless legs syndrome was suspected and we decreased the dose to 60 mg/day without improvement. From the 17th day after admission, when mianserin was decreased to 30 mg/day, she reported relief of the symptoms.

Discussion

The signs and symptoms of these patients almost fit the criteria of restless legs syndrome, as proposed by Gibb & Lees (1986).

The restless legs syndrome of our cases, however, needs to be differentiated from akathisia. Zubenko *et al* (1987) described the occurrence of akathisia associated with the administration of antidepressants: the patients exhibited syndromes characterised by motor restlessness and dysphoria that were clinically indistinguishable from either the idiopathic or neuroleptic-induced forms of akathisia. Although the relationship between akathisia and the restless legs syndrome is unclear (Blom & Ekbom, 1961), we think that our subjects' clinical features (symptoms predominantly confined to the lower legs (Gibb & Lees, 1986), becoming worse at night (Blom & Ekbom, 1961; Gibb & Lees, 1986), and disrupting sleep (Yassa *et al*, 1988)) favour the restless legs syndrome. Also, the fact that these patients did not report symptoms while on maintenance doses of amitriptyline for a considerable period is inconsistent with tricyclic-induced akathisia.

All three patients were treated only with mianserin. Furthermore, none of our patients had a history of neurological dysfunction, and their neurological examinations were normal. They were all otherwise medically stable and not suffering from conditions associated with the restless legs syndrome, such as iron-deficiency anaemia, uraemia, or diabetes (Clough, 1987). None of the subjects was pregnant. No personal or family history of the restless legs syndrome was identified. The symptoms remitted after mianserin was either discontinued (cases 1 and 2) or reduced (case 3). More importantly, we observed a return of the symptom with the reintroduction of the drug in case 1. Thus we think that the development of restless legs syndrome was associated with the administration of mianserin. However, the syndrome did not develop until the dose was 60–90 mg/day. Thus we postulate that the symptoms of restless legs syndrome might be related to dose, at least in some patients. The question of whether the syndrome was produced by the rapid increase in mianserin over a relatively short period will need further clarification.

The pathophysiological mechanism underlying the restless legs syndrome remains obscure, so it is conceivable that in a rare, susceptible patient, some neurochemical effect of mianserin may trigger this syndrome. More specifically, the development of this condition in response to mianserin as a norepinephrine potentiator (Goodlet *et al*, 1977; Rose *et al*, 1984) raises the possibility that noradrenergic mechanisms are involved. As experience with this drug widens and the number of patients who develop the restless legs syndrome after taking mianserin increases, these possible associations should be further clarified.

References

AMERICAN PSYCHIATRIC ASSOCIATION (1980) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn). Washington, DC: APA.

BLOM, S. & EKBOM, K. A. (1961) Comparison between akathisia developing on treatment with phenothiazine derivatives and the restless legs syndrome. *Acta Medica Scandinavica*, **170**, 689–694.

CLOUGH, C. (1987) Restless legs syndrome. *British Medical Journal*, **294**, 262–263.

GIBB, W. R. G. & LEES, A. J. (1986) The restless legs syndrome. *Postgraduate Medical Journal*, **62**, 329–333.

GOODLET, I., MIREYLEES, S. E. & SUGRUE, M. F. (1977) Effects of mianserin, a new antidepressant, on the in vitro and in vivo uptake of monoamine. *British Journal of Pharmacology*, **61**, 307–313.

MONTPLAISIR, J., GODBOUT, R., BOGHEN, D., *et al* (1985) Familial restless legs with periodic movements in sleep: electrophysiologic, biochemical, and pharmacologic study. *Neurology*, **35**, 130–134.

ROSE, A., MCCULLOCH, M. W., SARANTOS-LASKA, C., *et al* (1984) Effects of mianserin on noradrenergic mechanisms. *Journal of Psychiatry Research*, **18**, 79–87.

YASSA, R., ISKANDAR, H. & NASTASE, C. (1988) Propranolol in the treatment of tardive akathisia: a report of two cases. *Journal of Clinical Psychopharmacology*, **8**, 283–285.

ZIS, A. P. & GOODWIN, F. K. (1979) Novel antidepressants and the biogenic amine hypothesis of depression the case for iprindole and mianserin. *Archives of General Psychiatry*, **36**, 1097–1107.

ZUBENKO, G. S., COHEN, B. M. & LIPINSKI, J. F. (1987) Antidepressant-related akathisia. *Journal of Clinical Psychopharmacology*, **7**, 254–257.

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Contents: Interpretation of historical evidence/ Assessment of outcome/Toxicity of antidepressants/ Toxicity of hospital water?/Phobia and childhood parental loss/Flaubert's complaint/The damnation of benzodiazepines/Compulsory HIV testing in psychiatry/Delusions of pregnancy in men

Interpretation of historical evidence

Sɪʀ: May I reply to the letter of Persaud & Allderidge (*Journal*, May 1989, **154**, 719–720), criticising aspects of my paper on 'Schizophrenia as a recent disease' (*Journal*, October 1988, **153**, 521–531)?

Concerning Andrew Harper, it seems trivial to belittle his work on the ground that he had been an army surgeon. One might with better reason belittle Pinel on the ground that he had been a teacher of mathematics. Dr Persaud and Miss Allderidge have overlooked the fact that Harper (1789, pp vii, 9) defined insanity in terms of what we would now call the functional psychoses, and that he specifically excluded mental disorders due to bodily disturbances or toxins (Leigh (1961, p. 68), in criticising Harper's book, seems also to have overlooked this fact). If organic psychoses are excluded, then Harper's statement of insanity as being very rare in young people may properly suggest that adolescent schizophrenia was rare or absent in his time.

Harper's book was quoted with approval by Pinel (1801, p. 111 of the translation), and the adverse comments made in a footnote by his translator are dismissed by Cranefield (1962). Haslam's criticism of Harper (Leigh, 1961, p. 121) is specious, and perhaps reflects no more than his general quirkiness and his annoyance at Harper's assertion of the "ignorance and absurdity" of immediately confining victims of insanity to "the cells of Bedlam". Although limited in scope, Harper's book is straightforward and sensible and gives a good description (p. 68) of the intellectual deterioration associated with chronic mania, a condition much discussed during the 19th century and whose relation to schizophrenia has yet to be determined.

I can see no reason whatever to think that Haslam's evidence is 'more reliable' than Harper's. We know little of Harper's life, but we know enough of Haslam's (from the 1815 Select Committee) to know that his probity was not above suspicion. In any case, the statistics for admissions to Bethlem during 1784–1794 were not personally collected by Haslam, since he did not take up his appointment there until 1795; they were collected by his predecessor, John Gozna (Leigh, 1961, p. 103). At Bethlem, 'insanity' was used in its wider sense and included organic as well as functional psychoses (see Haslam's definition, 1798, p. 10). In citing the Bethlem statistics as evidence against the recency hypothesis, Dr Persaud and Miss Allderidge have overlooked this wider usage of insanity, for they seem to suppose that all young people admitted as 'insane' would have suffered from the 'adolescent insanity' described in the latter part of the 19th century. But it is much more likely that many, and perhaps most, of the young Bethlem patients suffered from organic psychoses, because the causes of organic psychoses – fever with delirium, encephalitis, head injury, vitamin deficiences, toxins, the effects of malnutrition, etc. – would have been far commoner then than now. Haslam (1809, p. 209) gives a list of such causes, and devotes a chapter (Ch. IV) to cases of "insane children", where he describes patients aged 3, 7, and 10 who evidently suffered from organic mental disorder.

Unlike Dr Persaud and Miss Allderidge, Wilkins (1987) was careful to point out that Bethlem admissions would not have been representative of the country as a whole. It is a pity that Wilkins confined his study to teenagers, for during the 19th century adolescence was generally taken as continuing up to the age of 25 (Clouston, 1892, p. 361). Thus Clouston (p. 362) says that developmental insanities occur most frequently during adolescence "from twenty-one to twenty-five". But so far from contradicting the recency hypothesis, Wilkins' study perhaps lends it some support. He found a significant increase with time in the proportion of patients having visual and auditory hallucinations; and whereas visual hallucinations are most commonly the consequence of fever, drugs, or toxins, the commonest cause of auditory hallucinations in young persons is schizophrenia.

Dr Persaud and Miss Allderidge are incorrect in saying that I argued that descriptions of recognisably schizophrenic symptoms are difficult to find at the beginning of the 19th century. What I said was that, on the recency hypothesis, "descriptions corresponding to adolescent insanity [in Clouston's sense of the term] will hardly be found in pre-1800 records"; and I said the earliest probable description I had found was in Cox's book of 1806 (the description is also given in his first edition of 1804). Their quotations from Haslam's books of 1809 and 1810 are therefore irrelevant as arguments against the recency hypothesis. Moreover, they fail to notice that I drew attention in my paper to the differences between Haslam's *Observations* of 1798 and his second edition of 1809. The remarkable passage in the second edition about "a form of insanity in young persons" does not occur in the first edition – that was my point. It is also noteworthy that Haslam says little about auditory hallucinations (and nothing about "voices") in his first edition (p. 5), but much more about them in his second edition (p. 68). In the second edition, but not in the first, he refers to 'the alarming increase in insanity'; and as late as 1843 he was still concerned with this increase, which he believed to be a real one (Leigh, 1961, p. 134).

Haslam's book of 1810 is entitled 'Illustrations of Madness, exhibiting a *singular* case of Insanity . . .' (my italics). Precise in his use of words and a student of etymology (Leigh, 1961, p. 116), Haslam would have chosen the word 'singular' with care. Its meaning was the same in his day (Johnson, 1807) as it is now – unique, extraordinary, unexampled, peculiar. Why then, we may wonder, should Dr Persaud and Miss Allderidge consider this case as an instance of what was 'so common, obvious and typical' as to be 'hardly worth mentioning'?

I am sure that many cogent arguments may be urged against the recency hypothesis, but I find little or nothing of substance in the criticisms of Dr Persaud and Miss Allderidge. And that leads me to think that the remarks in their final paragraph are out of place.

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References

Clouston, T. (1892) Developmental insanities. In *A Dictionary of Psychological Medicine*, Vol. I (ed. D. H. Tuke). London: Churchill.

Cox, J. M. (1806) *Practical Observations on Insanity* (2nd edn). London: Baldwin and Murray.

Cranefield, P. E. (1962) Preface to facsimile reproduction of *A Treatise on Insanity by Ph. Pinel*, trans. from the French by D. D. Davis. New York: Hafner.

Harper, A. (1789) *A Treatise on the Real Causes and Cure of Insanity*. London: Stalker.

Haslam, J. (1798) *Observations on Insanity*. London: Rivington.

—(1809) *Observations on Melancholy and Madness*. London: Callow.

—(1810) *Illustrations of Madness*. London: Rivington *et al.*

Johnson, S. (1807) *Dictionary of the English Language* (12th edn).

Leigh, D. (1961) *The Historical Development of British Psychiatry*. Oxford: Pergamon Press.

Pinel, P. (1801) *Traite medico-philosophique sur l'alientation mental.* Trans. (1806) by D. D. Davis as *A Treatise on Insanity*. Sheffield: Cadell and Davies.

Wilkins, R. (1987) Hallucinations in children and teenagers admitted to Bethlem Royal Hospital in the nineteenth century and their possible relevance to the incidence of schizophrenia. *Journal of Child Psychology and Psychiatry*, **28**, 569–580.

Assessment of outcome

Sir: Tarrier *et al* (*Journal*, May 1989, **154**, 625–628) report a substantial rate of "relapse" of schizophrenia after 24 months of aftercare that included 9 months of a specific psychological intervention as an adjunct to drug therapy. They comment that several other recent studies of psychosocial and drug combinations have shown an increase in psychopathology once the psychosocial intervention has been completed, and advocate the continuation of such treatment for a longer period. They fail to note that the one study that did follow this valuable advice not only showed continued low levels of schizophrenic and affective psychopathology, but also showed a substantially higher recovery rate, in terms of both the clinical condition and social disability (Falloon, 1985).

The preoccupation of schizophrenia researchers with preventing "relapse", a state poorly defined in most studies (Falloon *et al*, 1983), has led to a neglect of measurements that reflect the quality of life of the patient and his caregivers. I suggest that the aim of long-term management of any chronic disorder characterised by exacerbations and remissions should focus on maximising functioning and minimising handicaps, as well as controlling symptoms. A longitudinal approach that targets the continuing and changing needs of patients and their support systems seems essential. Continued targeting of psychosocial interventions as well as drug therapies may yet lead to an enhanced rate of clinical and social recovery from schizophrenia. The advocates of such a strategy are urged to conduct further studies to assess the long-term benefits of continuing optimal multimodel therapies.

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References

Falloon, I. R. H. (1985) *Family Management of Schizophrenia: a Study of Clinical, Social, Family, and Economic Benefits.* Baltimore: Johns Hopkins University Press.

—, Marshall, G. N., Boyd, J. L. *et al* (1983) Relapse in schizophrenia: a review of the concept and its definitions. *Psychological Medicine*, 7, 469–477.

Toxicity of antidepressants

Sir: Beaumont (*Journal*, April 1989, **154**, 454–458) has contributed in an imaginative way to the debate concerning the prescription of antidepressant medication. The principal issue reviewed in his article is that of toxicity in overdose.

A number of authors have addressed the issue of calculating the relative risk of fatal poisoning associated with antidepressants, notably Leonard (1986) and Cassidy & Henry (1987). While there is no definitive way of arriving at a calculation which will precisely predict the pattern of fatalities following overdosage with antidepressant agents (since the necessary data is unavailable), these authors provide a 'fatal toxicity index' which attempts to predict the number of deaths per million prescriptions of each drug.

The results are striking, and perhaps can be illustrated even more clearly by the extrapolations below. The total number of prescriptions for antidepressant medications in 1987, in the UK, was around 7 009 000 (Pers. Comm., ICI Pharmaceuticals). We can therefore use Cassidy & Henry's formula to predict that if only a single antidepressant agent were to be administered throughout the UK, we could expect the following consequences: exclusive use of dothiepin would result in 350 deaths per annum; amitriptyline, 326; and doxepin, 219. In contrast, use of the 'newer' antidepressants would compare as follows: trazodone, 95 deaths per annum; and lofepramine, 0. Since the body of evidence available would suggest little difference in efficacy between the spectrum of antidepressant agents, the justification for using the older, more toxic antidepressants seems tenuous. Additionally, the newer compounds have superior adverse effect profiles.

In the light of current political developments, we are likely to be subjected to progressively greater pressure to 'rationalise' our prescribing habits. Our fear is that this will involve the production of Regional Health Board and hospital formularies which will attempt to restrict our antidepressant prescribing to that of the cheapest products available. Already, in the Grampian area, we are being urged to use amitriptyline, imipramine, and doxepin.

We agree that there seems little need to use other than a small fraction of the antidepressant medications available to us. However, we suggest that restricting our clinical freedom to the use of lofepramine, trazodone, one of the serotonin re-uptake blockers, and a single MAOI (for example phenelzine) might substantially reduce the 'human cost' of our prescribing.

We are faced with balancing financial considerations against those of fatality in overdose. Since doctors are generally poor at predicting suicide attempts (Barraclough *et al*, 1974), it is currently inevitable that our patients will continue to kill themselves with the tools which we supply. Which is the greater cost?

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References

Barraclough, B., Bunch, J., Nelson, B., *et al* (1974) A hundred cases of suicide: clinical aspects. *British Journal of Psychiatry*, **125**, 355–373.

Cassidy, S. & Henry, J. (1987) Fatal toxicity of antidepressant drugs in overdosage. *British Medical Journal*, **295**, 1021–1024.

Leonard, B. E. (1986) Toxicity of antidepressants. *Lancet*, *ii*, 1105.

Toxicity of hospital water?

Sir: We have recently reported (King & Birch, 1989) that toxic concentrations of heavy metals in drinking water may occur at Victorian mental hospitals with independent water supplies. The problem is compounded by compulsive water drinking among chronically psychotic patients, which is often difficult to detect and is probably under-diagnosed (Noonan & Ananth, 1977; Lee *et al*, 1989). Heavy metal neurotoxicity masquerading as psychiatric illness seems a real possibility in some of our institutions, especially where maintenance has been neglected.

We are unsure how widespread such hazards are in practice, and should be interested in hearing from anyone working in older hospitals where discoloured water may indicate corroded pipework.

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References

King, J. R. & Birch, N. J. (1989) Health hazards on tap. *Lancet*, *i*, 1080.

Lee, S., Chow, C. C. & Koo, L. C. L. (1989) Altered state of consciousness in a compulsive water drinker. *British Journal of Psychiatry*, **154**, 556–558.

NOONAN, J. P. A. & ANANTH, J. (1977) Compulsive water drinking and water intoxication. *Comprehensive Psychiatry*, **18**, 183–187.

Phobia and childhood parental loss

SIR: The recent report by Tweed *et al* (*Journal*, June 1989, **154**, 823–828) that agoraphobia with panic attacks and, to a lesser extent, simple phobia in an adult community sample are associated with parental loss or separation in childhood is an important contribution to our understanding of the aetiology of phobic disorders. However, certain limitations imposed by their method, particularly as they affect the interpretation of the negative results, should be noted.

Any interview procedure that screens for categorical cases will inevitably misclassify a proportion of borderline subjects. So long as there is no consistent bias in favour of over or under-diagnosis, this misclassification will not affect the estimation of prevalence rates for a disorder. However, the presence of false positives in the case group will confound the search for factors associated with the disorder in question, and studies of correlates based on unmodified survey data are likely to underestimate the significance of any associations. This problem can be overcome in two ways, either by excluding borderline subjects from studies of correlates (Robins, 1985), or else by verifying the subjects' case/non-case status according to particular rules in a follow-up case-control study. The advantage of the latter strategy is that it allows a more sensitive estimation of the significance of associations, particularly if there is pairwise matching of cases and controls.

The findings of Dr Tweed *et al* have been derived from a simple comparison of screen-positive and screen-negative survey subjects. This probably does not detract from the significance of the association reported between phobic disorders and childhood parental loss; indeed, a more rigorous approach might have demonstrated a stronger link. Where this study may have failed to do justice to the data is with regard to possible associations between childhood parental loss and other disorders such as social phobia and generalised anxiety disorder, and between anxiety disorders and specific maternal or paternal loss.

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ROBINS, L. N. (1985) Reflections on testing the validity of psychiatric interviews. *Archives of General Psychiatry*, **42**, 918–924.

Flaubert's complaint

SIR: I was interested to read in a recently published biography of Gustave Flaubert (Lottman, 1989) that he suffered from epilepsy, probably of temporal lobe origin (Gastaut & Gastaut, 1982). The biography also contains ample evidence of Flaubert's compulsive promiscuity and passion for writing, which be described as his "idée fixe". In a letter to one of his many female lovers he remarks, "I write a love letter to write, and not because I love". His great interest in religious matters is well known to any reader of his works, which include *Herodias, La Tentation de Saint Antoine*, and *Legend de Saint Julian Hospitalor*. Of himself he once said, "One must live as a bourgeois and think as a demi-god".

Several authors, including Trimble (1986), have drawn attention to a specific interictal syndrome associated with temporal lobe epilepsy and consisting of disorders of sexual function, hypergraphia, and hyperreligiosity. It seems probable that Flaubert suffered from this syndrome, but unlike many other fellow-sufferers, he was a genius able to turn his own pathology into art.

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References

GASTAUT, H. & GASTAUT, Y. (1982) La maladie de Gustave Flaubert. *Revue Neurologique*, **6–7**, 467.

LOTTMAN, H. (1989) *Flaubert*. London: Methuen.

TRIMBLE, M. R. (1986) Hypergraphia. In *Aspects of Epilepsy and Psychiatry* (eds M. R. Trimble & T. Bolwig), pp 75–87. Chichester: Wiley.

The damnation of benzodiazepines

SIR: The paper by Kraupl Taylor (*Journal*, May 1989, **154**, 697–704) is timely. His use of the term 'anxiety illness' applies to most of the multitude suffering from various forms of disabling and often chronic anxiety. A look back to the condition of such patients before benzodiazepines became available about 30 years ago reminds us of the very unsatisfactory medication (e.g. barbiturates and amphetamines) commonly prescribed, not to mention the physical treatments and even psychosurgery resorted to in desperation by those seeking relief from intolerable anxiety. With the benzodiazepines, the improvement for many by way of the relief of symptoms was impressive. They were able to live "tolerable and reasonably normal lives, taking fairly full advantage of their abilities". Many were able to go out alone, travel, and hold down a job. Such patients were maintained for long periods on reasonable doses which did not need increasing. Disabling anxiety often returned if the dose was reduced, which is not surprising in patients suffering from those particular chronic illnesses.

Further distress is now occurring in this chronically anxious, and therefore vulnerable, group of patients as a result of the damnation chorus. While the benzodiazepines may be far from ideal, there is still a large population needing treatment for anxiety. This may have to be in the form of medication, even if only because the sheer weight of their numbers makes other forms of treatment unavailable.

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Compulsory HIV testing in psychiatry

SIR: The Royal College of Psychiatrists' guidelines for the management of HIV-related conditions in psychiatric practice were published recently (Catalan *et al*, 1989). The *British Medical Journal* commented that perhaps the most controversial point in the guidelines refers to the legality of testing without consent (*British Medical Journal*, 1989). The question, however, extends beyond the framework of the current legislation. The 1983 Mental Health Act was drawn up at a time when the HIV test was not yet available and the HIV epidemic was not a major issue on the British agenda. It would be wrong to use such legislation to support controversial clinical procedures which should be primarily driven by ethical, social, and clinical considerations. In the light of this *Journal's* coverage of these issues to date, I will concentrate on the points which merit further discussion.

1. Placing an emphasis on education and confidentiality when dealing with HIV in psychiatric practice is not an easy option, but is a challenge which could be met with alacrity. It is as well to ask how many psychiatric hospital wards give regular education programmes on AIDS-related risk behaviours to staff and patients, and how many provide ready access to condoms? In the face of staff prejudices, their knowledge of a patient's serostatus can lead to worse rather than better patient care (Cummings *et al*, 1986).

2. A difficult dilemma might arise in the future when AIDS-related dementia is suspected in a patient, now that treatment with zidovudine has become an experimental option (Schmitt *et al*, 1988). The evidence at present does not justify compulsory HIV testing and treatment with zidovudine in this condition.

3. I do not believe that HIV testing should be carried out without consent in patients showing aggressive or uninhibited behaviour. From the point of view of the patient, the financial, social, and occupational implications of an HIV test are enormous. Perhaps these need to be further spelt out to proponents of compulsory testing. It has been known in the past, for example, for an insurance company to penalise a candidate for having had an HIV test, whatever the result. From the point of view of staff safety, a negative result could "lull (them) into a false sense of security", as Dunn (1988) has already pointed out. A negative HIV Ab test can result not only from the sometimes lengthy period to seroconversion, but also from the finite specificity of the tests. It is important, therefore, to ensure staff safety by the provision of adequate numbers of trained staff and protective equipment.

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References

BRITISH MEDICAL JOURNAL (1989) HIV testing in psychiatry. *British Medical Journal*, **298**, 1600.

CATALAN, J., RICCIO, M. & THOMPSON, C. (1989) HIV disease and psychiatric practice. *Psychiatric Bulletin*, **13**, 316–332.

CUMMINGS, M. A., RAPAPORT, M. & CUMMINGS, K. (1986) A psychiatric staff response to acquired immune deficiency syndrome. *American Journal of Psychiatry*, **143**, 682.

DUNN, J. (1988) Screening for HIV. *British Journal of Psychiatry*, **153**, 568–569.

SCHMITT, F. A., BIGLEY, J. W., MCKINNIS, R., *et al* (1988) Neuropsychological outcome of zidovudine (AZT) treatment of patients with AIDS and AIDS-related complex. *New England Journal of Medicine*, **319**, 1573–1578.

Delusions of pregnancy in men

SIR: We read with interest Chaturvedi's report (*Journal*, May 1989, **154**, 716–718) of delusions of pregnancy in men. We describe below a patient with delusions of multiple pregnancy and multiple births where, unlike Dr Chaturvedi's case, no obvious organic pathology seemed to account for this symptom.

Case report: A never married, 31-year-old caucasian male with a 15-year history of chronic undifferentiated schizophrenia was admitted for in-patient evaluation after having failed to respond to adequate trials of three different neuroleptic drugs. He had also developed intolerable symptoms of akathisia and dystonia. All neuroleptic drugs had been discontinued one week prior to admission. Propranolol (80 mg/day) and lorazepam (1.5 mg/day) were discontinued over a period of 7 days after admission.

On admission, the patient's mental state revealed multiple somatic and grandiose delusions, in addition to thought broadcasting, third person auditory hallucinations (short sentences, mood-incongruent, both conversing and commenting voices), and marked thought disorder. One of his unshakable morbid beliefs was that he had been pregnant ("with four boys and a girl") and that he had delivered quintuplets a year ago in a hospital. He was convinced that while pregnant he could feel pressure on his abdomen and ribs and that "babies were kicking about". He believed that his internal organs had been traded with those of a woman, and hence he had a uterus. He believed that he had impregnated himself. His affect was restricted in its range. He was fully oriented with normal memory.

The patient had been born after 42 weeks gestation by breech presentation, after prolonged labour (48 hours). He developed pneumonia and febrile convulsions at 18 months, which did not recur. His developmental milestones were normal, and he passed all his school grades up to age 16, when in a period of weeks his grades dropped dramatically, and he developed psychotic symptoms leading to his first psychiatric admission. He has had eight subsequent admissions to psychiatric hospitals. Despite many trials of neuroleptics over the years, his positive symptoms had been refractory to treatment. His family history is notable for psychiatric illness among second-degree relatives (endogenous depression, epilepsy, and schizophrenia). There was no history of drug or alcohol abuse.

Physical and neurological examinations were essentially normal, as were blood biochemistry (including thyroid, liver, and renal profiles), urinalysis, routine haematology, and a computerised tomography scan and EEG. Following treatment with clozapine (300 mg/day) for 4 weeks, his thoughts were more organised, his hallucinations were less frequent and he was more sociable. However, he remained firm in his belief of having been pregnant and of having delivered quintuplets.

While no gross cerebral pathology was detected, we cannot rule out subtle cerebral dysfunction in view of the history of perinatal complications and febrile convulsions. Like Dr Chaturvedi, we were unable to demonstrate any disturbed family dynamics, a postulated pathogenetic factor in this symptom complex. At a psychopathological level, we wonder whether the preoccupation with bizarre somatic delusions (he believed that his ribs had been "eaten" and replaced, and that organs had been substituted) had led to secondary somatic hallucinations (pressure in his abdomen and ribs, babies moving about), as had been suggested by Hamilton (1976). On the other hand, it may be that somatic hallucinations occurred first and secondarily led to somatic delusions, as it was difficult to get the patient to correctly sequence this symptom, which he had had for approximately 4 months prior to this admission. He displays a retrospective delusion in that while he no longer believes he is pregnant, he backdates his delusion to a year ago, whereas he has held this belief for 4 months.

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HAMILTON, M. (1976) *Fish's Schizophrenia (2nd edn)*, pp 45–46. Bristol: John Wright.

SIR: We were most interested to read the paper by Chaturvedi (*Journal*, May 1989, **154**, 716–718). We should like to report a further case.

Case report: The patient was an unmarried 33-year-old caucasian man. He was born prematurely at eight months with Fallot's tetralogy, which was successfully corrected at the age of 11 years. He is of borderline intelligence (WAIS score 70). He attended ESN (M) (educationally subnormal-mild) school between the ages of 5 and 15, and then worked as a road sweeper until his first episode of psychosis at the age of 23. It is reported that at that time he heard voices saying that he was a poof, a woman, and that he was masturbating. He was sure that he was pregnant, and was in hospital "to have a vagina put on him".

There was no evidence of clouding of consciousness and he had no insight into his symptoms. He was treated with phenothiazines and ECT, with marked improvement, but his symptoms did not completely resolve. Over the next 8 years he continued to receive psychiatric care from general psychiatrists, both as an out-patient and at times as an in-patient, receiving a diagnosis of schizoaffective psychosis.

The patient was admitted recently because he had jumped out of an upstairs window. At interview he expressed his usual paranoid delusions that people were wishing to kill him. He also expressed a firm belief that he was pregnant. When it was pointed out to him that men do not become pregnant, he answered that he knew this but there was always a first time. He was quite concerned about how the baby would be born, as he had no vagina. He thought he had become pregnant by masturbating.

The patient is 5′ 5½ tall, obese, with normal genitalia, and has a girlfriend with whom he has a sexual relationship. Investigations showed normal chromosomes and normal biochemistry. His current medication consists of flupenthixol decanoate injections (60 mg every three weeks) and chlorpromazine (50 mg twice per day).

Dr Chaturvedi's patient was of low intelligence, with an IQ of 42; our patient had an IQ of 70, and unlike Dr Chaturvedi's, did not suffer from epilepsy.

Evans & Seely (1984) have reported pseudocyesis in a male who, like our patient, had a diagnosis of schizoaffective disorder.

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Reference

EVANS, D. L. & SEELY, T. J. (1984) Pseudocyesis in the male. *Journal of Nervous and Mental Disease*, **172**, 37–40.

CORRIGENDUM

Journal, June 1989, **154**, 754–767 (L. Eisenberg). In the footnote on p. 754, *'and Communication in Medicine'* should be deleted.

A HUNDRED YEARS AGO

"Is instrumental delivery a cause of idiocy".

To the Editors of THE LANCET

SIRS,—In your issue of Jan. 5th, under the above heading, reference is made to a paper in a Dutch medical journal by Drs. Winkler and Bollaan on the "Forceps as a Cause of Idiocy", and it is stated that "they are disposed to think that the use of forceps is much more frequently the origin of idiocy than is generally supposed". I am afraid that if this statement is allowed to go forth to the profession uncontradicted, great harm will result; for the researches of those of us who are engaged in the training and treatment of idiots and imbeciles prove that the use of the forceps has much less influence than their disuse in the production of idiocy and imbecility. I have for some years taught the students, who are sent here by some of the lecturers on psychological medicine, that prolonged and difficult labour is a potent cause of imbecility, and that in such conditions it is better to put on the forceps than to run the risk of prolonged compression of the head, resulting in asphyxia, paralysis, and other evils. Of course, one supposes that the forceps will be put on carefully. I have lately been inquiring into this very subject, and, putting aside the predisposing causes of intemperance, insanity, imbecility, epilepsy, &c., which are often present, I find that of 810 cases, in which I have been able to obtain histories, only thirty-five, or 4.3 per cent, are said to be due to the application of forceps, while 216, or 26.6 per cent, are due to the prolonged and difficult labour. Further, the majority of these cases, when born, were not only asphyxiated, but were in a helpless condition, some having lost the use of their legs, others becoming subject to convulsions. Moreover, the head was often crushed, elongated, discoloured, and deformed. On the other hand, in the thirty-five cases which had been delivered by forceps, only seven were helpless or paralysed. I therefore maintain that the use of the forceps is preferable to prolonged and difficult labour, and I would ask the profession not to be mislead by the few cases of Drs. Winkler and Bollaan.

I am, Sirs, yours faithfully,

FLETCHER BEACH

Darenth Asylum for Imbecile Children, Jan. 7th 1889.

Reference

The Lancet, 12 January 1889, 97.

Researched by Henry Rollin, Emeritus Consultant Psychiatrist, Horton Hospital, Surrey

British Journal of Psychiatry (1989), **155**, 425–429

Books Reconsidered

The Myth of Mental Illness: Thomas S. Szasz*

Thomas Szasz is one of the most disliked names in contemporary psychiatry, and *The Myth of Mental Illness* is one of the most disapproved of books. It was Szasz's contention that illness can affect only the body and that there can be no such thing as an illness of the mind. He described mental illness as a metaphorical illness, maintaining that one can speak of a 'sick' mind only in the same way as one can speak of a 'sick' joke or a 'sick' economy. He went on to argue that, if there is no mental illness, there can be no treatment for it, and no cure of it. There was, for him therefore, no medical, moral, or legal justification for involuntary psychiatric intervention or hospital admission. Such actions he considered to be crimes against humanity. He believed, after John Stuart Mill, that a man's body and soul are his own and not the state's, and that each individual has the right to do with his body whatever he pleases so long as it does not harm anyone else or infringe anybody else's rights.

Szasz's respect for human liberty may, in part, be the result of his youth being spent in an increasingly threatened part of Europe. In 1938, following the Nazi occupation of Austria, his family, who lived in Budapest, left Hungary for America. He was aged 18 and, shortly afterwards, entered the University of Cincinnati, from which he graduated with honours in physics. He is now almost 70, but still speaks with a Hungarian accent. In his book he observed that speaking a language with a foreign accent is like having a transference reaction. In such a reaction one person behaves towards another as though he were someone else previously familiar to him. His move from Hungary to America, at this critical time, may account for his subsequent preoccupation with language and with communication.

Szasz moved progressively further away from physics, the study of inert objects and natural laws, to a concern with what he termed man's sign-using behaviour. He qualified in medicine at the age of 24, entered psychiatry two years later, and between the ages of 27 and 30 underwent psychoanalytic training. It is important to understand that, although he is often critical of Freud, he is seriously committed to psychoanalysis and has always maintained a private practice for voluntary fee-paying patients.

His contention was that what psychoanalysts and other psychosocially-orientated psychiatrists do is communicate with patients by means of language, non-verbal signs, and rules. Beyond this, they analyse, by means of verbal symbols, the communicative interactions which they observe and in which they themselves engage. For this reason he believed that psychiatry has much in common with the sciences concerned with languages, sign-using, and communication. There is, in Szasz, a polarisation between his first love, physics, and his later preoccupation with communication. It is this which lies at the heart of his distaste for the medical model of psychiatry. In fact, it was his enthusiasm for such disciplines as symbolic logic, semiotics, and sociology which caused him to deplore the reliance of psychiatry on what he considered to be the outmoded conceptual framework of organic medicine. The conceptual scaffolding of medicine, he argued, rests, quite reasonably, on the principles of physics and chemistry; but these have no relevance for his behavioural or interactional conception of psychiatry.

The Myth of Mental Illness, Szasz's first book, was written with great passion, and the ideas expressed in it were clearly pressing to be let out. He began it at the relatively early age of 34, when he was called to active duty in the US Navy and when he was relieved of the burden of a full-time psychoanalytic practice. He was appointed to the chair of psychiatry at the Upstate Medical Centre of the State University of New York in Syracuse, at the age of 36, before he submitted the book for publication. Within a year of its publication, the Commissioner of the New York State Department of Mental Hygiene demanded, in a letter which specifically cited the book, that Szasz be dismissed because he did not "believe" in mental illness. He survived, although some of his supporters were less fortunate. In an interview in 1972 he confessed that he continued to teach orthodox psychiatry to his students in much the same way as an atheist might teach comparative religion (Sabbagh, 1972).

It is useful to draw parallels between Szasz and the psychologist Timothy Leary, whose seminal work *The Interpersonal Diagnosis of Personality* was published in 1957. Within Leary's book there were remarks which were every bit as contentious as those of Szasz, but either because his book had a more respectable title, or because he was a professor of psychology and not of psychiatry, he was able to get away with them. In the end, however, he suffered a worse fate than Szasz: he was expelled from his post at Harvard for continuing to advocate the use of psychedelic drugs. Szasz and Leary had both been influenced by the psychoanalyst Harry Stack Sullivan, whose own book *The Interpersonal Theory of Psychiatry* was published in 1953. Szasz drew freely on Sullivan's game model in explaining hysterical behaviour. The inspiration for much of Leary's research derives from Sullivan's belief that the field of psychiatry is the field of interpersonal relations. Leary considered that Sullivan had convincingly buried the much-berated remains of descriptive, Kraeplinian and negatively-value-toned psychiatry, but had provided no substitute system of classification. He devoted himself to rectifying this omission and predicted that "within a few decades" direct interpersonal terms would replace what he called "the disorganised nosology of present day psychiatry".

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*New York: Hoeber-Harper (1961).

There is clearly an anti-authoritarian component to the personalities of both Szasz and Leary, and both have a need to challenge the established order of things. At the same time, both have a redeeming, constructive side to them. Szasz' criticisms of orthodox psychiatry feature mainly at the beginning and the end of his book. Once he had got these off his chest, he settled down to a sober and serious account of various alternatives to the medical model. It is not widely known that the book carries the sub-title *Foundations of a Theory of Personal Conduct*. Like Leary, he stated that he had two objectives. The first was what he called a "destructive" analysis of the concept of mental illness, and of psychiatry as a "pseudo-medical enterprise". The second, and to my mind by far the more important, was the presentation of a "constructive" synthesis of the knowledge which he had found useful in filling the gap created by the shedding of the "myth of mental illness".

The theme which runs throughout the book is Szasz's struggle to come to terms with the diagnosis of hysteria. In fact, had his iconoclastic zeal been less fervent, a more suitable title for the book might have been "Problems in the diagnosis of hysteria". This would have won him more friends and gained him less notoriety. He referred to hysteria as a paradigm of mental illness, and maintained that everything he said about hysteria would, in principle, equally apply to all other "so-called mental illnesses". In fact, hysteria is a most unusual condition, and is far from what one might select to represent a typical mental illness. It belongs to a kind of no-man's-land between a physical and a mental condition, for although the patient presents with physical symptoms he does so for psychological reasons. The condition was deliberately chosen by Szasz because it so admirably suited his purpose, and the book is, I think, one of the best accounts of the possible mechanisms which lie behind the hysterical process.

One of Szasz's most consistent and compelling arguments is that an illness is something which happens to someone, i.e. something which one has. The illness takes over or inhabits the person's body. The function of the clinician is to work on this thing inside the person, to dispel it or to bring it under control. What disturbed Szasz about orthodox psychiatry is that it induces in the patient a passive attitude – that he simply lets the doctor get him better. This also applies, he felt, to classical psychoanalysis. In his opinion, most so-called mental illnesses are not something which one has, but something which one does. This distinction is perhaps not always as clear cut as he would have us believe. Many who suffer from recurrent, severe affective disorders would be in no doubt that these are things which happen to them, although it must be conceded that, whatever it is which does happen to them, it in turn causes them to do things, such as hide themselves away from others or give their possessions away. There are, of course, physical illnesses which cause patients to do things (the choreas, for example), although what they cause them to do are not of an interpersonal nature. The principle, however, has considerable relevance for psychiatry, for it implies that patients are, to a large extent, responsible for their thoughts, words, and actions, and therefore should play a more active and responsible part, with the support of the therapist, in resolving their problems. It has especial relevance for hysteria, in which the patient presents himself or herself as being helplessly in the grip of some physical condition but is, in fact, actively deciding to take on the condition, i.e. he or she is actively deciding to be passive!

Szasz laid great emphasis on the fact that the hysteric chooses to play the role of a sick person because sick people get looked after in our society. Like the infant's cry, the message, "I am sick" is exceedingly effective in mobilising others to some kind of helpful action. In the hysterical transaction, disability is used as a coercive tactic to force others to provide for one's needs. The hysteric would not adopt his particular posture if there were not those who are prepared to respond to it in a helping way. The helpers thus hasten to the side of the helpless. In the wild, the animal who pretends to be sick is either attacked or ignored. Szasz argued that within civilised societies there are understandings that it is acceptable to be weak and needy. One such understanding derives from religion. Should man be sick, help-seeking, poor, and humble, God will care for him and protect him; God will forgive him, help him, love him, and allow him to be passive and incompetent. Also, there are people within society who derive satisfaction from helping the needy. The parent who rewards his child's persistent helplessness and dependency in order to enhance his own importance and self-esteem is one such person.

Szasz considered that the physicians follow in the footsteps of their predecessors, the priests, in responding to the call of the sick. What passes for medical ethics, he claimed, is a set of paternalistic rules, the net effect of which is the persistent infantilisation and domination of the patient by the physician. He accused Freud of a similar attitude, maintaining that he insisted that the psychoanalytic relationship between analyst and analysand must be that of a superior and a subordinate. He did not seem to regard genuine co-operation between equals as either possible or desirable. One suspects, therefore, that what lies behind Szasz's objection to psychiatric conditions being called illnesses is that this induces a one-down, helpless attitude in patients and a one-up helping attitude in psychiatrists. His inclination is clearly towards a co-operative endeavour between patient and therapist which maximises the patient's choices in the conduct of his life.

What many psychiatrists find so confusing about Szasz is that he appears to be denying the existence of what so obviously do exist, namely mental illnesses. In fact, he does not deny the existence of the various diagnostic conditions, and quite freely writes of them. He simply chooses not to call them illnesses. Psychiatrists then counter with: if he acknowledges their existence, what does it matter what he calls them? It matters a great deal, because what one calls something is an indication of what class of phenomenon one considers it to belong to, and this determines how one responds to it. Quite early in the book Szasz made it clear that he considers diagnostic categories to be forms of communication, similar in certain respects to languages. Here again, hysteria fits into this class of phenomenon more easily than do certain other diagnostic categories. He maintained that it is pointless to think in terms of a cause or a treatment for a language. Instead, it is necessary to understand why the person chooses to speak in such a language and what he is trying to say in it. What makes hysteria such a challenge for Szasz is that the language the patient chooses to speak in is what he calls "the language of illness". Although he chooses to speak in the language of illness, he clearly is not ill.

For Szasz, interpreting the language of hysteria is similar to Freud's method of interpreting a dream. The choice of symptom is important, since this may be a clue to what the patient is trying to say. Szasz warned against trying to render the symbolism of the hysterical symptom into the more concrete form of ordinary language. There is a parallel here with Freud's distinction between the primary process of dreams and the secondary process of grammatical, logical speech. Szasz further warned that the hysteric's message may have been intended for an internal object, and not for the person who actually receives or tries to interpret it. A further feature of hysterical communications is that, like dreams, they may have a number of meanings all condensed into one.

The important question to ask about the communication of the hysteric is why does he not say what he needs to say straight out; why does he have to resort to such a roundabout form of communication? There are two obvious answers to this. The first is that indirect messages permit communicative contact when, without them, the alternative would be total inhibition, silence, and solitude; the second is that more direct communication might be offensive or forbidden. The indirect communication therefore has a protective function. By being ambiguous, the communicator is only hinting at a delicate issue, and may be able to disown both to the recipient or to himself the true content of the message. It could be said that the hysteric cannot afford to be aware of what he is doing, for if he were he could no longer allow himself to do it.

Considerations such as these led Szasz to describe the hysteric as both a liar and a cheat. He observed that psychiatrists are reluctant to use such blunt terms; once a person is called a patient, the psychiatrist somehow is unable to think in terms of deception or mendacity. This he believed is regrettable, since it signifies the contemporary psychiatrist's sentimentalising attitude towards those they consider to be mentally ill. Szasz would insist that it is essential to be clear about the hysteric's intention to deceive before it is possible to understand and subsequently to help him. While it does not seem that the hysteric carefully plans his strategy, it is a mistake, he contended, to emphasise the unwitting quality of his behaviour. 'Conscious' and 'unconscious' are terms with which Szasz is never comfortable, since they detract from the principle that, at all times, the patient is aware of, and carries responsibility for, what he is doing.

In order to explain why the hysteric needs to resort to lying and cheating, Szasz drew upon games theory.

In fact, as the book progressed he moved away from considering mental illnesses as languages towards considering them as forms of game playing. This set them more into a social context, and implied that psychiatric patients have motives for their actions, i.e. that there is method in their madness. It is here that he felt that Sullivan had the edge on Freud, for Freud largely continued to relate to the patient as though he were ill, to consider that the pathology resided within him, and to encourage the patient to adopt a passive, regressive attitude. Phrased in terms of game-playing, the hysteric is someone who would gladly take advantage of cheating if he believed he could get away with it. He plays at being sick because he is afraid that if he tried to participate competently in certain real-life activities he would fail. His cheating is so staged as to lead those around him to interpret it not as a selfish stratagem but as unavoidable suffering. Viewed as a game, hysteria is characterised by the goal of domination and interpersonal control. The typical strategies employed in pursuing this goal are coercion by disability and illness.

One important feature of game playing is that it takes more than one person to play a game. A patient cannot continue to play his particular game unless the significant others with whom he interacts play the same game by the same rules. In one illustrative case, Szasz described a woman who found that the simplest and most effective way that she could cope with her oppressive, unreasonable, and intrusive mother was by lying. The discovery that her mother would accept her lies without openly challenging them encouraged her use of this strategy, and eventually lying became established as characteristic features of her personality. Szasz wrote, "As both she and I familiarised ourselves with the type of game she was playing, it became increasingly evident that the people to whom she lied knew, most of the time, that she was lying. And of course, she did too". He went on, "Her husband ostensibly accepted her lies as if they were truths and then used his knowledge that they were falsehoods to manipulate her in his own interests". Ideas such as this are very much a part of the theory of present-day family therapy.

Viewing mental illness, and in particular hysteria, as a form of game playing has considerable implications for therapy. By adopting a particular symptom, or complex of symptoms, the patient has adapted as best he can to his particular life situation. It is important to be respectful of this, and to appreciate the usefulness of the symptom for him. The psychiatrist whose sole aim is to free the patient of his symptom may be ignoring any consideration of how this might affect his adjustment to life. It could equally be argued that a patient may not be prepared to relinquish his symptom unless he can see a way of adapting to his circumstances without it. Szasz suggested a number of possible directions in which the hysteric might move. These include more effective coercion or domination of others; greater submission to others and increased preoccupation with suffering; or withdrawal from the struggle over interpersonal control by progressive isolation from real life relationships.

These last suggestions bear a striking resemblance to the kind of thinking which lay behind Leary's interpersonal classification of behavioural styles. Since, in their separate books, Szasz and Leary made no reference to each other, it seems likely that, although both were inspired by Sullivan, they reached their respective positions via independent routes. Adams (1964) effected a useful synthesis of the two approaches. Starting from the premise that mental illness is not a health or medical problem but a phenomenon involving interpersonal behaviour, he proposed that programmes of alleviation and prevention must rest on a systematic understanding of interpersonal conduct. He then drew attention to a body of recent research which indicated that all interpersonal behaviour, whether adaptive or maladaptive, could meaningfully be categorised within one systematic frame of reference. This was organised around Leary's two dimensions of dominance-submission and affection-hostility. Fifteen years later, McLemore & Benjamin (1979) made a further significant contribution by proposing a general method for translating traditional diagnostic categories into psychosocial terms which avoided what they termed "continued endorsement of a disease conceptualisation of abnormality by being explicitly constructed in terms of psychosocial behaviours". Over the past decade, research in the interpersonal field has made considerable progress, and Kiesler (1986) concluded a comprehensive review with the statement, "Systematic interpersonal diagnosis is an increasingly viable and practicable option".

There was therefore in Szasz's book the germ of an idea, which, had it been more modestly presented, would have contributed to an interesting debate. He tended to spoil his case by being such a mischief-maker. It seems likely that there was something of the mischief-maker in Leary too. Between them, they may have held back progress in the interpersonal field. Hopefully, more sober researchers are now making up the lost ground.

References

Adams, H. B. (1964) Mental illness or interpersonal behaviour. *American Psychologist*, **19**, 191–197.

KIESLER, D. J. (1986) Interpersonal methods of diagnosis and treatment. In *Psychiatry, Vol. 1* (ed. J. O. Caveman), pp 1–23. New York: Lippincott.

LEARY, T. (1957) *The Interpersonal Diagnosis of Personality*. New York: Ronald.

MCLEMORE, C. W. & BENJAMIN, L. S. (1979) Whatever happened to interpersonal diagnosis? *American Psychologist*, 34, 17–34.

SABBAGH, K. (1972) The boy from Syracuse. *World Medicine*, 4 Oct. 1972.

SULLIVAN, H. S. (1953) *The Interpersonal Theory of Psychiatry*. New York: W. W. Norton.

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Book Reviews

Editor: Sidney Crown

The Child Molester: An Integrated Approach to Evaluation and Treatment. By GEORGE W. BARNARD, A. KENNETH FULLER, LYNN ROBBINS and THEODORE SHAW. New York: Brunner/Mazel. 1989. 288 pp. $27.50.

Lasting Effects of Sexual Abuse. Edited by GAIL E. WYATT and G. J. POWELL. London: Sage. 1989. 288 pp.

Once can see from these two works that, despite the burgeoning of what amounts to an industry in child sex abuse publications, uncertainties still abound and legal and therapeutic policies remain matters of controversy.

Shaw directs an evaluation and treatment centre in Florida for prisoners who volunteer and are assessed as suitable for treatment as mentally disordered sex offenders. Men appealing against sentence, suffering from major psychiatric disorder, or insufficiently motivated to change are all excluded. The therapies made available to these selected individuals are remarkably comprehensive, including behavioural techniques (such as masturbatory satiation), a variety of group methods (such as 'interpersonally oriented' groups), social skills training, meditation, sex education, abreaction, autobiographical analysis, and relapse prevention exercises.

As is often the case in this difficult area, objective evaluation of outcome is hardly mentioned. The effectiveness of sex-suppressant drugs is reviewed in one chapter, but this is one form of treatment not mentioned in connection with the Florida regime. Therapeutic optimism is sustained by an eclectic view of aetiology which sees child molestation as the behavioural outcome of a multiplicity of influences. Whereas some offenders have poor impulse control, perhaps combined with substance abuse, others may have difficulty in relating to adults. Others again may have heightened sexual arousal to children, possibly conditioned by early sexual experiences, and some may have hormonal abnormalities or inhibitions derived from sexual traumata. A variety of therapeutic methods tailored to individual needs offers the best chance of modifying offending behaviour.

The early chapters give a brief review of victim surveys, offender confessions, and historical studies, all of which point to a high prevalence of adult-child sexual contacts. It would seem, therefore, that measures applied to the small minority of cases selected for treatment following detection and prosecution can have little effect on what happens in the community at large, but no such conclusion is drawn by these authors. They do, however, review some of the social and legal barriers to therapy. "The therapist who works with sex offenders is sometimes regarded by others as a sex offender advocate" (p. 241). The law's commitment to adversarial methods and black and white categorisation conflicts with the more qualified nature of clinical assessments (p. 207). Clinicians may be caught between a duty of confidentiality to the patient and a duty to protect potential victims. All 50 states of the US have reporting laws which require suspected child sexual abuse to be reported to the authorities (p. 216).

The compilation edited by Wyatt & Powell contains more academically-oriented reviews of research. Temporary as well as lasting effects of abuse are discussed. Disagreement about what constitutes abuse (for instance whether there has to be an age gap between offender and victim, whether the activity has to be unwanted or forced, whether actual physical contact has to occur, and what age range is covered by 'child') accounts for many of the discrepancies in research findings. Clinical studies, based on referrals of children requiring treatment following disclosure of traumatic sex abuse, usually by adults in their own homes, yield a different picture from community surveys in which most remembered incidents of 'abuse' are casual encounters outside the home.

A remarkable variety of disturbances have been linked with history of sex abuse in childhood. They include drug addiction, anxiety attacks, bad temper, 'out-of-body' experiences (p. 87), depression (p. 112), negative life experiences (p. 126), guilt, schizophrenia (p. 145), antisociality (pp. 145, 166), and sexual delinquency (p. 201). The confusing complexity of these relationships is beginning to be realised. Family pathology may contribute both to the likelihood of abuse and to subsequent disturbance. The nature and quality of the sexual incidents (such as the age when they occur, whether they are one-off or repeated, the child's temperament and emotional development, the relationship to the offender, and the gender of offender and victim) are all relevant to both short and long-term impact.

The last chapter, on implications for clinical practice, is a useful corrective to simplistic rules of procedure for what are in reality very different situations. Boys, for example, who are more often victims than was once thought, tend to react differently from girls and probably more aggressively. In their case molestation usually involves anxiety-provoking homosexual implications. Assessments of disturbance in victims need to be more systematic, so that symptoms specifically related to adverse sexual experience can be distinguished from a 'pot pourri' of complaints arising from other causes. Premature sexualisation, routinely attributed to abuse, can sometimes follow unsupervised exposure to videos (p. 275). Treatment evaluations are "not methodologically stringent enough to know what really works and why" (p. 278). Finally, risk of exposure to AIDS adds new dimensions to the potential damage of penetrative sexual abuse.

D. J. West, *Institute of Criminology, University of Cambridge*

Affective Disorders. Edited by Frederic Flach. New York: W. W. Norton. 1989. 238 pp. £21.50.

This is the third volume in the *Directions in Psychiatry* monograph series. Its distinguishing features include an exceptionally open and balanced introduction from its editor, many widely differing theoretical perspectives, and a sustained emphasis on the clinical application of research findings.

The book comprises 19 brief articles ranging from women and suicide, and pharmacotherapy of the depressed alcoholic, through sleep deprivation, and depression and the immune system, to seasonal affective disorder, and the place of family therapy in the management of affective illnesses. Each begins with a short editor's summary which points to the clinical relevance of what follows. Most chapters involve researchers describing their own area of special interest, and some show a lack of editorial control in that their literature reviews are unbalanced, out of date, or even misleading. The quality appears at times almost as variable as the many theoretical standpoints adopted, but nevertheless all are thought-provoking, and taken together they form an impressive array of departure points for further 'directions' in the 1990s.

Anthony Storr's outline of the principles of psychotherapy with depressed patients is masterly, although he has written as well, if not better, on this topic elsewhere. This latter observation applies also to the chapters on cognitive therapy, antidepressant plasma levels, misdiagnosis of physical illness, and Keller's account of the USA Collaborative Depression Study; but here in one volume is a convenient starting point for the illumination of many of those dark corners that one feels one ought to know at least a little more about than one can remember. A book to borrow when any of its 19 fascinating topics beckon, or when the routine of treating depressed patients begins to pall, but not one to rely on for the correct answers to any MCQ.

Alan S. Lee, *Consultant Psychiatrist, University Hospital, Nottingham*

Causes, Coping and Consequences of Stress at Work. Edited by Cary L. Cooper and Roy Payne. Chichester: John Wiley. 1988. 430 pp. £29.95.

This comprehensive review of research literature on many aspects of stress at work is part of a large series. The editors express the hope that it will appeal to many groups in medicine, industry, psychology, etc., but I feel that those who will find it most useful are people looking for specific research data (e.g. family influence or computer stress); it works better as a literature review than as a general book that will give simple ideas to apply in the clinic or workplace. The world literature is enormous, so for the wider public it would have been useful if the editors had attempted to draw together a general synopsis for those who are not in full-time stress research. As a doctor I would have found this valuable to relate the details of each chapter to a central hypothesis.

There is a helpful "stress or strain" model (p. 11), and some chapters deal with part of the paradigm presented, but this only appears in a section on epidemiology, and is not used elsewhere. This model does emphasise the clash between factors produced by the workplace (noise, workload, automation, personal demands, pace) with those relating to personality and social factors, but I would expect to use the word 'intrinsic' to include all the variations of the individual and family, and 'extrinsic' to deal with the industrial side.

An interesting concept is Karasek's 'demand-discretion' model, which highlights the increased stress that results for any worker whose employment creates demands on time, speed, or effort, but does not give them any chance to make any decisions about the workload. This explains why there can be high levels of stress in people who do simple repetitive labour, as well as in some complex levels of management. This has been related positively to coronary heart disease episodes. A 'demand-support-constraints' model (Fletcher & Payne) may be more useful within a single industry. A major problem in this kind of research is the lack of totally reliable objective indices that a person is under too much strain.

The "merger syndrome" is interesting as a study of the effect on all levels of a company when a takeover is due, and many observations are recorded on the effect of this type of threat. There is also a useful exploration of issues related to the strain of working with computers. Chapter 4 gives a searching synopsis of the findings, whereas the previous one gives little critical analysis of the many papers quoted.

The most practical advice occurs in pp 304–305, where specific ideas are put forward on methods of reducing work stress as identified by unions and management, and on p. 271, which suggests concrete methods of promoting health. For those considering research in these difficult subjects the final chapter on research design is very useful.

TED CANTRELL, *Senior Lecturer in Rehabilitation, Southampton General Hospital*

Serotonergic Mechanisms in Anxiety Disorders. An Inquiry Into Serotonin Function in Panic Disorder. Edited by J. A. DEN BOER. Amsterdam: Duphar. 1988. 232 pp.

Hippocrates delineated pathological forms of anxiety in the 5th century BC, and Cicero made a distinction between *angor* and *anxietas* many centuries before the introduction of DSM–III. Anxiety disorder, however, received serious medical attention only at the end of the 19th century. According to the author, during the last few decades relatively homogeneous subgroups of anxiety disorders have been identified in which different types of anxiety symptoms dominate the clinical picture. One of these, panic disorder, has been studied more thoroughly than the others. The core of the book is concerned with the question of whether or not there are serotonergic abnormalities associated with panic disorder.

After giving a historical sketch of the origins of the concept of anxiety disorders, diagnostic categories as in DSM–III–R are discussed. That panic disorders form a distinct group within the anxiety disorders and have a greater validity makes the task of the researcher easier.

In chapter 3, determinants of vulnerability for anxiety disorders and neurobiological theories relating specifically to panic disorder are discussed. In the subsequent chapters several studies concerning the serotonin function in panic disorder are presented, e.g. biological concomitants of lactate-induced panic attacks, and a double-blind comparison of clomipramine and fluvoxamine. Both the latter are potent drugs in panic disorder; this is probably related to their 5-HT uptake-inhibiting properties. Maprotiline, a selective noradrenaline reuptake blocker, was found to be ineffective in reducing the number of panic attacks, thereby supporting the serotonin hypothesis.

In practice, during the first two weeks of treatment with 5-HT uptake inhibitors the symptoms of panic disorder show a transient increase. Hypersensitivity of 5-HT_2 receptors could be an explanation for this phenomenon. However, the studies in the book could not confirm this hypothesis.

There is increasing evidence that 5-HT uptake inhibitors are therapeutically effective in the treatment of panic disorder. According to the presented studies, there is some support for the existence of a dysfunctional serotonergic neuronal system in panic disorder. In the field of rapidly growing data on the serotonergic system, this is a most valuable book for theory and practice alike.

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Computer Psychotherapy Systems: Theory and Research Foundations. By MORTON WAGMAN. New York: Gordon and Breach Science Publishers. 1988. 261 pp. $68.00.

Wagman is a mathematically-inclined psychologist who has developed a simple counselling technique administered by computer. The subject reformulates his problem as a series of dilemmas and then examines logically the horns of each dilemma. In this book Wagman reports his studies showing the effectiveness of such counselling in volunteer students, and discusses more generally the use of computer-based 'expert systems' in counselling.

This is preceded by discussion of the theoretical basis of computer-administered counselling and psychotherapy. He introduces the concept of artificial intelligence, describes approaches to language analysis, and comments on the important elements of different psychotherapies. He evaluates earlier work, including the well known 'client-centred' ELIZA program which operates merely by reformulating clients' comments according to strict rules.

A key idea about artificial intelligence is Turing's test of thinking, which elegantly sidesteps philosophical uncertainties by asking the empirical question of whether or not the computer's appearence of thinking can be distinguished from a human's thinking. Circumscribed elements of human thinking can be mimicked credibly by computer. For example, PARRY, a program which answers like a paranoid individual, does so well that a group of psychiatrists interviewing via teletype could not distinguish PARRY from real paranoid patients.

Many psychotherapists would think the notion of computer psychotherapy a joke. But it is not too difficult to see how the elements of behavioural therapies can be instrumentalised. That a computer program could handle psychoanalytic therapies is more difficult to accept. Wagman does produce an interesting discussion of transference to a computer psychotherapist. However, his comments on computer countertransference (which deny it as a possibility) are disappointingly shallow, and he seems unprepared to explore some of the more complex issues that might arise if artificial intelligence does begin to move closer to human intelligence.

Most of the book is well set out and easy to follow (despite some tortured prose), with plentiful references.

However, I was disappointed by the failure to develop discussion of any topic very far, by the lack of detail in the survey of previous work, and by the lengthy and repetitious presentation of the author's own work.

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Family Abuse and its Consequences: New Directions in Research. Edited by Gerald T. Hotaling, David Finkelhor, John T. Kirkpatrick and Murray A. Straus. London: Sage. 1989. 318 pp. £14.95 (pb), £35.00 (hb).

Coping with Family Violence: Research and Policy Perspectives. Edited by Gerald T. Hotaling, David Finkelhor, John T. Kirkpatrick and Murray A. Straus. London: Sage. 1989. 323 pp. £14.95.

Each of these books contains 21 research papers, selected from more than 400 presented at a conference on family violence at the University of New Hampshire. The authors include social scientists, psychologists, psychiatrists, paediatricians, lawyers, criminologists, and community physicians, and their contributions survey aspects of family violence in all parts of the United States.

Failure to report a known or suspected case of child abuse is a criminal offence in the USA, as, sadly, it is not in Britain – can this be, at least partly, the reason why maltreatment of children appears to be several times more frequent in the USA? In England and Wales about 40 000 children, or 0.35% of the population at risk, are on child protection registers. The corresponding proportion in the USA is reported as being between 1% and 2%, or more than a million children.

Inevitably, given such statistics, non-accidental injury of children features extensively in these volumes. It features, however, by no means exclusively. Violent behaviour between marital partners, between courting couples ("date abuse"), and against aged dependents ("elder abuse") is also covered, as is sexual molestation.

All the expected aetiological relationships emerge from these pages: the self-perpetuating cycle of violence where offspring, it seems, are doomed to assert their own identity, status, and self-esteem by emulating abusive parents; the subcultures where abuse is a desperate form of non-verbal communication; the young mothers unsupported, or with partners who are not their children's fathers; the unrealistic parental expectations resulting from widespread ignorance about normal child development; the individual childhood experiences, superimposed upon educational and social class attitudes, determining which 90% of Americans consider physical punishment an acceptable sanction, and which 10% do not; the malign influence of substance abuse; and the essentially haphazard occurrence of the occasional tragedy. As the New York Mayor's Task Force found during its 1987 investigation of child deaths from abuse or neglect, "the fatal and non-fatal cases belong to a common pool... in which fatality is primarily a chance outcome".

Family Abuse and Its Consequences is mainly descriptive. *Coping With Family Violence* is partly descriptive – especially with reference to motivation and rationalisation, for example contrasting male and female attitudes within abusive relationships – but also investigates individual and organisational attempts at amelioration. There is a paper about group therapy for wife-batterers, and another about the shelter movement. There is an illuminating contribution by a lawyer on police attitudes to domestic violence. The difficulty of predicting serious child abuse is discussed frankly, as is the near-impossibility of statistical evaluation in a field where no control case, unless retrospective, can ethically exist.

The 42 papers inevitably vary in clarity, style, and forcefulness. Criticism of earlier research in the USA is over-detailed for readers elsewhere. Some authors include abstracts or summaries; others do not. It is possible, but quite difficult, for a non-American reader to identify the disciplines and qualifications of contributors described in an appendix only, and there mainly with reference to their previous publications. Each paper has an extensive bibliography, but the work as a whole has no index.

Such small reservations notwithstanding, these volumes represent an important contribution to an urgent study, and should certainly be in our libraries.

Margaret J. Little, *Associate Specialist, Division of Psychiatry, Stobhill General Hospital, Glasgow G21 3UW*

Cognitive Foundations of Clinical Psychology. By Chris R. Brewin. London: Lawrence Erlbaum Associates. 1988. 214 pp. £8.95 (pb), £24.50 (hb).

During the past decade, the dominant orientation of clinical psychology has switched from the behavioural to the cognitive, but this movement seems to have emerged in a piecemeal fashion, lacking a clear theoretical basis. Brewin's book is to be welcomed, therefore, as the first textbook to review and integrate the cognitive theories underlying the practice of clinical psychology. This is a bold venture, and one can't fail to be impressed by Brewin's grasp of a wide literature which he presents in a thorough and scholarly manner.

Cognition is described as being concerned with *knowledge*, and Brewin states that "the theme of knowledge and its acquisition will be central to this book". Yet there is not a single reference to knowledge in the index, and readers expecting a substantive consideration of the role of knowledge in human experience will be disappointed. Instead we are taken through a diverse selection of topics in which cognitive processes have been investigated. These include the unconscious, conditioning, affect, attribution, expectancies, and goals. There is also a consideration of information processing in anxiety and depression, and a chapter on cognition and interpersonal relationships. The book ends with a chapter on therapy, where it is argued that cognitive change may be common to a wide variety of therapeutic procedures.

Although the book is primarily academic in nature, Brewin does make some use of clinical examples, and the book will undoubtedly be of value to those clinicians who wish to discover more about the theoretical and empirical basis of cognitive approaches to treatment. Although it is clearly written, I found it rather dry and uninspiring in style. I was also disappointed by the failure to address the historical and social factors behind the current cognitive emphasis of clinical psychology. Nor did I come away from the book with any sense of integration. This, however, may be less a criticism of Brewin than of his subject matter. The cognitive approach seems just as disparate as the behavioural movement in its heyday.

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Modern problems of Pharmacopsychiatry: Volume 23. Diagnosis and Treatment of Old Age Dementias. Edited by H. E. LEHMANN and T. A. BAN. Basle: S. Karger. 1989. 109 pp. £32.80.

This volume presents the proceedings of a symposium on the diagnosis and treatment of old age dementias held in Milan in 1987. The title is rather an exaggeration, as the book is dominated by discussions of the importance of cerebral blood flow, even in Alzheimer's dementia, and the value of drugs which influence it, with little reference to much else. The theme of the book is really ateroid (glycosaminoglycan polysulphate, which affects blood rheology) and not dementia. The grand title and cover diagrammatic representations of sequences of glycosaminoglycans (GAGs) promises a sophisticated appraisal of extremely important subjects, but little in the book lives up to expectation. It comprises five chapters introducing aspects of diagnosis and investigation, two dealing with the biochemistry and pharmacology of GAGs (especially ateroid), and three reporting findings from clinical trials of ateroid.

The first two chapters on diagnosis are brief and flimsy. Similarly, the chapter on neurotransmitters barely touches on the subject, but the sections covering neuroimaging and neurophysiology (including topographic brain mapping) are quite concise and contain some helpful plates. There follows a description of the structure and biological activity of mammalian GAGs, which will appeal more to the biochemist than clinician although it does explain effectively what they are. The pharmacological profile of ateroid is clearly and concisely described, and gives us reason to believe it should be a useful substance.

The final chapters describe three clinical studies of ateroid purporting to provide research evidence of its efficacy in treating the symptoms of chronic organic brain syndromes. The first, a small, uncontrolled, open study, shows very modest benefits for Alzheimer's dementia but not for multi-infarct dementia, which could be explained by non-drug effects. The second, a small double-blind placebo-controlled study, shows positive effects with multi-infarct dementia (astonishingly, no placebo patient was rated improved, while 12 of 15 ateroid-treated patients were – what happened to the placebo effect?), and the final study contains so many major methodological weaknesses as to render the results almost meaningless.

Overall there is little to recommend in this book, although the occasional chapter has some merit. The title promises more than the book delivers; it has little relevance for the practicing clinician, is too limited to assist the trainee, and lacks the sophistication required by the researcher or academic. The clinical studies reported here do little to convince this reader of the clinical value of ateroid.

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Essential Psychiatry. Edited by NICHOLAS ROSE. Oxford: Blackwell Scientific. 1988. 277 pp. £122.95.

This sturdy paperback, slightly larger than A4 in format, is edited by the clinical tutor in psychiatry at Oxford and written with 14 of his colleagues. Its claimed purpose is to provide an introduction to "the range of topics relevant to someone working in the mental health field, whether they be social worker or GP, medical student or nurse". In practice, medical students are likely to form the majority of its readership. There are several books available to medical students at a similar price; is the one we should be recommending?

Each chapter starts with a 'factsheet', forming a synopsis of what follows, and ends with a list of essay questions and an annotated further reading list. The text is not otherwise referenced. There are no photographs and only occasional line diagrams, but extensive use is made of highlighting and of boxes to include both key and optional points. Differences between general medicine and psychiatry are well explained in the introductory chapter on diagnosis and classification, with extensive use of illustrative cases. ICD–9 and DSM–III are mentioned but not DSM–III–R. Research strategies and the inter-relatedness of genetic, biological, social, and psychological models of psychiatry are elegantly introduced in Hope's chapter on causation.

The account of patient assessment emphasises interviewing skills and the information necessary to make a systematic formulation. Little reference is made to the need for corroborative evidence, and the section on mental state examination gives no guide to normal range or to the need to standardise cognitive assessments. Of the subsequent chapters on specific conditions, that on affective disorders is clearest, with a good account of clinical features and a balanced review of treatment strategies, but little discussion of diagnostic criteria or epidemiology. Schizophrenia is treated somewhat more impressionistically and, suprisingly, the list of Schneiderian first rank symptoms is incomplete. In the section on neurosis, behavioural treatments are well described, but benzodiazepines are referred to as "safe and effective anxiolytics", although their dependency potential is also mentioned. Organic states receive eight pages of description and no account of management. A wide-ranging chapter on general practice and hospital psychiatry provides the only reference to eating disorders, and dismisses peurperal psychiatry in less than a column. An excellent synopsis of old-age psychiatry presents the demographic background, and the section on dementia appropriately concentrates on the range of presenting problems and of available services. Late paraphrenia, however, goes almost unmentioned. Towards the end of the book there are predictably good accounts by Hawton on suicide and Cowen on physical treatment, as well as a balanced and humane discussion of bereavement and related problems by Stedeford. Hawton's other contribution, on sexual problems, emphasises the dysfunctions with only scanty mention of sexual deviation.

Overall, *Essential Psychiatry* is good on assessment and relatively weak on management. It would also be much strengthened by clearer reference to existing diagnostic systems. The book's main strength lies in its unwavering focus on the needs of an undergraduate readership. This alone makes it an important contribution to available undergraduate texts. It also means that our students will buy it whatever we tell them. I think they could do a lot worse.

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Cities of Tomorrow. By PETER HALL. Oxford: Basil Blackwell. 1989. 473 pp. £25.00.

Cliches of Urban Doom and Other Essays. By RUTH GLASS. Oxford: Basil Blackwell. 1989. 266 pp. £25.00.

In case readers of this *Journal* query the value of reviewing two books on town planning in a journal of psychiatry, we need only go back a hundred years to London's East End to see the squalour, overcrowding, and misery of unplanned urban life. Even today the burden of psychopathology is strikingly high in certain inner-city estates, and this is only in part accounted for by drift.

The problem is essentially that the wealth created by cities draws in poor from outside, each additional arrival producing extra strains on accommodation and transport such that it would more than pay current residents to support that individual elsewhere. As, however, choices are made by individuals or by families, some form of rationing has to be introduced with controls on building. *Cities of Tomorrow* is an excellent account of cities of the past, taking chapter by chapter different movements which have attempted to solve the problems of urban crowding. Naturally chapters tend to overlap both in time and planners, as few planners were as single-minded as Corbusier. Sadly, the first solutions often seem to have been the best, such as the green belt, the muncipal housing of Unwin before the war, and the garden city movement. Later chapters concern the regional development typified by the Tennessee Valley Authority, the grandiose city designs of pre-war dictators, the high-rise towers to which central government tripled the subsidy which was given to other types of housing; the restoration movement (e.g. Covent Garden), the growth of motorways and satellite towns, free enterprise schemes (e.g. Docklands), and finally the problems of the continuing slum breeding grounds for crime, with absence of rewards for productive work. Hall writes well, and this book is an excellent introduction to understanding our urban environment, helping to make us aware, if we did not already know it, that our urban planners do not have the solution. The future of psychiatry demands that they quickly find one.

Ruth Glass is another distinguished academic and town planner, and her short book is a collection of essays and lectures given over 50 years. As each essay is complete in itself, they inevitably tend to cover the same issues, frequently for example criticising the notion, as put forward by the Chicago group, that social malaise can be attributed to housing conditions. Curiously, despite her academic negativism she holds firmly to the idea of the benefits of muncipal housing, passing over the tower block fiasco as if it was a minor hiccup on the ability of local authorities to plan for all varieties of men. A committed socialist, she blames most of the world's ills on capitalism and ignores the ability of the private market to build houses that people want. Much better are her chapters on racial minorities, in which she describes with great sympathy and insight the problems of disadvantaged groups and argues persuasively for laws banning racial abuse. However, unlike the more positive book by Hall, one comes away from this book with no clear principles for town planning except that the local authority knows best!

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Annotation

The Classification of the Depressions
Contemporary Confusion Revisited

ANNE FARMER and PETER McGUFFIN

It is 13 years since Kendell (1976) reviewed the 'contemporary confusion' surrounding the classification of depression. Reconsideration of this issue is now timely, especially in light of the development of the new classifications of affective disorder included in DSM–III (American Psychiatric Association, 1980), the revised version, DSM–III–R (American Psychiatric Association, 1987), and the forthcoming ICD–10 (World Health Organization, 1988). Recent activities in neurobiological, genetic and social research also bear importantly on our concepts of the aetiology of depression.

In 1976 the approaches advocated by nosologists varied considerably: some subdivided depression into one or two subtypes (Lewis, 1934; Carney *et al*, 1965) while others proposed multiple different categories (Blinder, 1966; Paykel, 1971). Kendell suggested that only two approaches to the subdivision of affective disorder would be of future relevance: firstly to divide depression into endogenous/psychotic 'type A' and reactive/neurotic 'type B' subtypes; and secondly to follow Leonhard (1959) with a distinction between bipolar and unipolar illness. Kendell also suggested that a bipolar/unipolar subdivision would become increasingly important with the emphasis on the biological basis of affective disorder in research. Finally, Kendell considered that the concept of involutional melancholia had outlived its usefulness, and soon afterwards this diagnosis was omitted from ICD–9 (World Health Organization, 1978). Kendell acknowledged that different workers were likely to continue employing different nosologies, but also stated that there should be an insistence that each classification be accompanied by unambiguous operational criteria and specifications of the terms used.

In this paper, we consider the changes in the classification of depression that have taken place since Kendell's review. In particular we examine the use of operational definitions as exemplified in DSM–III and other North American classifications and ICD–10. Finally, we consider whether these changes represent progress in our understanding of the nosology of depression or whether they merely provide a different variety of 'contemporary confusion'.

The reliability of diagnosis and operational definitions

The problems concerning the reliability of diagnosis that occupied researchers in the 1950s and '60s led to the suggestion (Stengel, 1959; Hempel, 1961) that the use of operational criteria would help to overcome nosological difficulties in psychiatry.

Operational definitions were first suggested for use in physics by Bridgman (1927), but in suggesting their application in psychiatry, Hempel (1961) stated that certain modifications would have to be made to the original concept. This included a more liberal interpretation of the term 'operational'. What has commonly resulted is an approach described, perhaps somewhat disparagingly, as a Chinese menu. A number of criteria must be present to fulfil the operational definition of disorder, but within each criterion a choice is available. In general, the structure of each operational definition of depression follows the same basic format. Firstly, the mood state is identified (e.g. dysphoric or depressed mood), followed by a symptom list of a number of different items which must accompany low mood (early morning waking, suicidal ideation, poor concentration, etc.). Next a 'duration' criterion is included which varies between definitions; for example the Research Diagnostic Criteria (RDC) specify one week (Spitzer *et al*, 1975), the St Louis criteria one month (Feighner *et al*, 1972) and DSM–III two weeks. Lastly, there are one or more exclusion criteria. All criteria exclude depression due to organic mental disorder and some also exclude affective disorder accompanied by prominent schizophrenic symptoms.

In addition, each of the sets of American operational criteria for depression embody different subtyping features. In particular, the RDC not only differentiate between primary and secondary depression but also between 'definite' and 'probable' diagnostic certainty. Moreover, the RDC also include criteria for eight subtypes of the disorder, including melancholia. This has probably contributed to the popularity of the RDC and their associated structured interview (Schedule for Affective Disorder and

Schizophrenia – SADS) in research use, particularly among biological psychiatrists who quest after homogeneous, aetiologically 'pure' subcategories.

DSM–III criteria for affective disorder were heavily influenced by both forerunners, the St Louis criteria and RDC. In addition, DSM–III was the first classification to group all affective disorders together and was also the first to abandon the traditional terms 'psychotic' and 'neurotic'. In order to maintain some comparability with ICD–9, a four-digit numbering system was used to identify disorder, but in addition a fifth-digit subclassification was introduced specifically for national use.

The DSM–III, criteria proved to be a landmark in the classification of affective disorder. For the first time, not only were operational definitions specified for use in research but their use clinically as recommended by the American Psychiatric Association was subsequently widely required for health insurance purposes. The fifth-digit subclassification allowed major depressive illness to be described as (a) in remission, (b) with melancholia, and (c) with psychotic features, specifying whether these are 'mood congruent' or 'mood incongruent'. In DSM–III, 'mood incongruent psychotic features' means delusions or hallucinations whose content does *not* involve personal inadequacy, guilt, disease, death, nihilism, or deserved punishment. Therefore, the term includes persecutory delusions, and symptoms such as thought insertion, thought broadcasting, and delusions of control, which most British psychiatrists would consider highly suggestive of schizophrenia. DSM–III–R includes more subclasses using the fifth digit. As well as grading severity of symptoms (mild, moderate, and severe, with or without psychotic features) partial and/or full remission can be specified. Full criteria for a melancholic subtype and seasonal pattern of affective disorder are also now operationally defined. In contrast with the other operational criteria for major depression mentioned above, DSM–III–R no longer makes it a mandatory requirement for the patient to admit to or complain of depressed mood.

Classification of depression in the *International Classification of Diseases*

ICD–8 (World Health Organization, 1974) was produced following a large survey of the state of psychiatric classification undertaken by Stengel (1959) (for historical background see Jablensky (1988)). Unlike the precisely defined syndromes of DSM–III, ICD–8 contained only brief clinical descriptions as guidance for the user. The novel feature of ICD–8 which represented an advantage over its predecessors was the international adoption of a glossary for definitions of mental disorders. The range of diagnostic categories for depression was increased in ICD–9 (1978). Unlike in ICD–8, an attempt was made to combine all depression categories under one group, a trend that has continued with the proposals for the tenth revision. In ICD–10 the four-digit numerical classification is to be replaced by alphanumeric codes. All psychiatric disorders are contained in Chapter V and are coded with the prefix 'F'; for example affective illnesses are placed in the F3 category.

Despite this new numbering system, the most recent (1988) draft of ICD–10 closely resembles DSM–III–R operational criteria for major depression and its subtypes. In ICD–10, depression categories in F3 are F31, single depressive episode, F32, depression occurring as a current illness within the context of bipolar disorder, and F33, recurrent depression. The old term 'manic-depressive psychosis' has been dropped in favour of the Leonhardian term 'bipolar disorder', but this is also in line with DSM–III and DSM–III–R.

Within these broad categories, depression is subdivided according to severity (mild, moderate, and severe) and types of symptoms (somatic or psychotic). Thus mild and moderate depression is described as with or without somatic symptoms, and severe depression as with or without psychotic symptoms. Somatic symptoms as listed in ICD–10 are almost the same as the operational criteria for the melancholia subtype of depression in DSM–III–R. Psychotic symptoms in ICD–10 are also described as mood congruent and incongruent according to the same criteria as DSM–III–R. Thus, like DSM–III, ICD–10 will allow some Schneiderian first-rank symptoms of schizophrenia to occur within a depressive disorder category (e.g. severe depression with psychotic symptoms and mood-incongruent delusions, F31.31, F32.51, F33.33). F34 includes persistent affective states (e.g. cyclothymia or dysthymia). Other types of affective episodes are categorised under F35.

Omitted from F3 are organic depressive states, post-schizophrenic depression and mixed anxiety and depression which appears in the neurotic disorder (F4) group. Schizoaffective disorder appeared in F3 in an earlier draft of ICD–10. However, in the most recent (1988) draft, schizoaffective disorders are placed once more in F2 (schizophrenia, schizotypal and delusional disorder).

The glossary for ICD–10 will appear with four different sets of guidelines (Sartorius, 1988): firstly, clinical diagnostic guidelines (c.f. ICD–9); secondly, diagnostic research criteria similar in format to the operational definitions currently in use in North America; thirdly, a multiaxial system which will enable patients' problems to be identified along different axes (e.g. (i) major psychiatric diagnosis, (ii) personality disorder, (iii) physical health problems, etc.); and fourthly, a short guide for use in general health care settings. As with the most recent draft of the clinical guidelines, the provisional diagnostic research criteria for depressive categories within ICD-10 and those for major depression in DSM-III-R are highly comparable.

The effect of the increasing application of operational criteria upon psychiatric nosology

Since 1976 the use of operational criteria in psychiatric nosology has become more influential than perhaps Kendell had envisaged. Although their use in research to improve diagnostic reliability is now well established, the introduction of their use clinically by the American Psychiatric Association is beyond Kendell's (1976) vision. Indeed, this extension of their application raised certain nosological issues which may be occultly changing our view of psychiatric illness. While this may be of only moderate importance in research it becomes much more important when operational criteria are used for clinical diagnosis and treatment or to provide national statistics about psychiatric disorder. ICD-10 will almost certainly clearly differentiate between research and clinical guidelines, while DSM-III-R uses the same criteria in both contexts. Let us, therefore, consider some of the issues that the application of operational criteria raises.

The use of operational criteria in clinical practice: a two-dimensional approach

Psychiatrists use many sources of information to arrive at a clinical diagnosis and these are often excluded in the approach to diagnosis that the use of operational criteria inevitably imposes. In particular, operational definitions usually take limited account of informant information, being heavily dependent on subjective symptoms. There is a clear-cut distinction between disorder and personality which is appealingly tidy, but clinically can often seem arbitrary. Context and the patient's social and cultural background are largely ignored, and compliance with and response to treatment are set aside. Thus, operational definitions of depression are inevitably constrained and somewhat 'two dimensional'. In addition there may be a tendency (there is certainly a temptation) among clinicians to use clinical judgement to make a diagnosis first and to fit the patient to the criteria second. This we can describe as a 'Procrustean bed' error after the practice of the Greek innkeeper of legend to suit his guests to the size of a particular bed by either stretching them or cutting pieces off to fit. This *post-hoc* method of using operational definitions would certainly be contrary to the spirit with which Hempel suggested they be introduced into psychiatry.

'Top-down', 'bottom-up' classificatory systems

The classificatory procedure imposed by the use of operational definitions also causes some limitations and constraints. These, however, do not pertain to other methods of classification employed in psychiatry (e.g. the PSE/CATEGO system; Wing *et al*, 1974; Wing & Sturt, 1978). Operational criteria rigidly impose pre-set diagnostic rules from the top down and the clinician has to decide whether an individual case fulfils these rules or not. Because of this rigidity, the operational criteria inevitably fail to assign a diagnosis to some patients, as they fail to fulfil all criteria, and who, therefore, become 'not yet diagnosed'. This is dealt with by the creation of miscellaneous 'rag bag' categories which inevitably become more full than with a more flexible diagnostic approach encouraged by the ICD-9 clinical guidelines and the CATEGO system.

In the latter, classification is approached from the bottom up, with the identification of a patient's symptoms. Symptoms are grouped into syndromes, and syndromes into subclasses. Finally a single most likely CATEGO class is assigned. This method of classification is more flexible, with a greater variety of clinical presentations being incorporated under the same diagnostic heading. This in turn reduces the numbers in the miscellaneous, 'rag bag' groups.

Diagnostic hierarchies

Most operational criteria have no inherent hierarchy in contrast with common clinical practice where implicit hierarchies are frequently employed. The use of exclusion criteria imposes a sort of hierarchy on the diagnosis of depression in DSM-III (the syndrome must not be superimposed on either schizophrenia, schizophreniform disorder, or paranoid disorder, and must not be due to organic mental disorder or uncomplicated bereavement). However, the authors of DSM-III-R have stated their intention to remove these because "studies have shown that research and clinical practice would be improved by eliminating many of the diagnostic hierarchies that have prevented multiple diagnoses when different syndromes occur together in the same episode of illness" (American Psychiatric Association, 1987). This, therefore, means that subjects who fulfil criteria for major depression may simultaneously fulfil criteria for generalised anxiety and panic attacks, and in such a case there are no rules built into DSM-III-R concerning the primacy of any one diagnosis.

In research, primacy rules can be applied by the investigator and may vary according to the type of research being carried out (e.g. first occurring temporarily, the most severe clinically, etc.). However, the absence of a diagnostic hierarchy in clinical practice poses many more problems, and the classification of patient populations has implications for both national health care statistics and management. The multidiagnostic approach runs counter to the rules of logic, as usually applied in the classification of diseases. According to Kendell (1975), these rules state that "abstract classes should be mutually exclusive and jointly exhaustive; i.e. that each class member possesses the defining attributes of one class only and possesses none of the attributes of any other class". While classification in psychiatry fails to achieve this logical ideal owing to the overlapping of symptoms between diagnostic groups, a hierarchical approach does at least allow for the assignment of a single diagnostic category for each subject. The use of operational criteria as implemented in DSM-III and DSM-III-R fails to do this.

Implicit in other nosologies (Wing *et al*, 1974; Foulds & Bedford, 1975) has been the supremacy of schizophrenic symptoms over those of affective disorder; for instance, in CATEGO (Wing *et al*, 1974), Schneiderian first-rank symptoms 'trump' other symptoms and the patient (providing he does not have organic psychosis) is firmly placed in the schizophrenia class (S+). However, DSM-III and DSM-III-R and the most recent draft of ICD-10 allow some core schizophrenic symptoms such as thought insertion and thought broadcast within the context of an affective disorder, for example in 'major depression with mood incongruent psychotic features'. Thus the supremacy of schizophrenic features in a diagnostic hierarchy is not observed.

With the increasing international influence of the DSM-III and DSM-III-R there will surely be a shift of the boundary between the major psychoses. This will clearly have a major impact on research into the major psychoses as well as upon national statistics, since many patients previously diagnosed as schizophrenic will be liable to be reclassified under a category of affective disorder.

Validity

The last major criticism of the use of operational criteria is that, although they can be used with good reliability (Farmer *et al*, 1983; McGuffin *et al*, 1984), without knowing the precise aetiology of depression their validity remains in question. Until this fundamental question is answered, operational definitions, like all other nosologies, remain hypothetical. Therefore, if a single diagnostic system is allowed to dominate our thinking we limit our nosological options and narrow the chances of finding the cause(s) of the disorder. A polydiagnostic approach has been suggested by several authors (Kendell, 1975; Katschnig & Berner, 1983) and we endorse this. If multiple sets of criteria are applied to the same subjects over the same period of illness, greater diagnostic flexibility can be achieved. In our view, for the time being this is essential.

Aetiological factors

Robins & Guze (1970) suggested an indirect approach to the validation of psychiatric disorder by employing clinical studies, laboratory tests, family studies, and outcome studies. Research in depression in recent decades has largely been polarised into those investigating the neurobiology of affective disorder (including twin and family studies) and those primarily concerned with environmental influences on the mood state (life events, adversity, etc.). A brief review of recent literature reveals that among neurobiologists there is virtual unanimity favouring the use of a unipolar/bipolar subgrouping. There is now a substantial body of evidence which has found that unipolar and bipolar subgroups of the disorder differ on a number of measures, for example prolactin and cortisol correlations (Joyce *et al*, 1988), prolactin rhythms (Halbreich *et al*, 1979), urinary 3-methoxy-4-hydroxyphenolglycol levels (Muscettola *et al*, 1984), plasma norepinephrine (Roy *et al*, 1985), plasma alpha$_2$ receptors (Kafka, 1986), cerebrospinal-fluid prostaglandins (Linnoila *et al*, 1983), glucose uptake on positron emission tomography (Phelps, 1984; Buchsbaum, 1986), and verbal memory deficit (Wolfe, 1987). The studies provide some evidence that Kendell's (1976) suggestion about the future importance of the unipolar/bipolar distinction has been borne out. However, there are interesting data from family studies suggesting that these disorders differ only quantitatively, both occupying the same multifactorial liability continuum (Gershon *et al*, 1982; Tsuang *et al*, 1985).

The neurotic/reactive, endogenous/psychotic subdivision still persists, particularly among researchers interested in the social aspects of depression (Parker *et al*, 1988). Clinical psychiatrists distinguish between endogenous and reactive subtypes of disorder on the basis of characteristic symptoms and of the relationship with potential psychosocial stressors. While there is still some lingering support for this traditional dichotomy, an increasing body of research evidence now fails to sustain such a sub-division. A number of researchers have attempted to validate the concept of endogenous depression. Andreasen *et al* (1986) employed family history of mental illness in depressed probands as a method of validating four different definitions of endogenous depression. They failed to find any increase in depression among the relatives of patients with endogenous v. a non-endogenous illness. Young *et al* (1986), from the same group, examined the internal construct validity of an endogenous subtype of major depression, using symptom ratings on 788 patients with major depression, from the National Institute of Mental Health Collaborative Depression Study. Once again the results did not support dichotomous melancholic/non-melancholic or endogenous/non-endogenous classifications. This multivariate statistical procedure suggested that there were two subtyping variables among depressed patients, one related to anhedonia and another to vegetative symptoms. The authors noted that the vegetative subtype rarely occurred in non-anhedonic patients. This implies that the subdivision was dimensional rather than categorical. More recently, results from the Camberwell Collaborative Depression Study (Bebbington *et al*, 1988; McGuffin *et al*, 1988*a*,*b*) failed to show any differences in levels of antecedent adversity between subjects rated as having neurotic depression and those with endogenous depression according to the CATEGO classification. Except when a very narrow definition of illness was taken, both forms of depression appeared to show equal degrees of familiality. In addition, the authors found no inverse relationship between the presence of family loading and reactivity to stress, and no apparent tendency for life-event-related depression to breed true in families (McGuffin *et al*, 1988*b*). Thus, it remains to be seen whether the endogenous/reactive subdivision of depression will retain its current credibility or whether, like 'involutional melancholia', this subtypology has outlived its usefulness.

One unexpected finding in the Camberwell study was that the tendency to experience (or to report) life events appeared strongly familial. Over a three-month period life events were four times more common in first-degree relatives of depressives than in the general population. Moreover, there was only a modest and non-significant association between recent life events and depression at time of interview in the sample of relatives (McGuffin *et al*, 1988*b*). One possible interpretation is that at least part of the often reported association between encountering life events and reporting depressive symptoms is that both are predisposed to by a common familial factor.

Conclusions: new directions or continuing confusion?

Certain of Kendell's suggestions regarding future directions have been borne out while others have not. Firstly, subdividing the disorder according to a unipolar/bipolar split has become accepted by most neurobiologist researchers of depression. Secondly, involutional melancholia did indeed decline and has been removed from the ICD system, but in DSM-III-R the concept of melancholia has returned (albeit in a different guise), invigorated with full operational criteria. Subtyping depression according to endogenous and reactive subtypes is still employed widely but much recent research has cast doubt over its future importance. Unmentioned by Kendell (1976) is 'seasonal affective disorder' which appears in DSM-III-R but not in ICD-9 or ICD-10. Lastly, the influence of operational definitions of depression has probably exceeded Kendell's original vision. Their use in research has become widespread, in fact virtually mandatory for reports aiming to be published by reputable journals. However, we suggest that the pendulum may have swung too far in this direction. The application of explicit operational criteria in everyday clinical practice magnifies the inherent nosological difficulties and becomes an abuse rather than a legitimate use.

What developments would be desirable in the near future? The formal adoption of the final draft of ICD-10 by the World Health Organization is due in 1992, along with its international use around the world, as well as the publication of DSM-IV. DSM-III-R is already exerting a strong influence on ICD and this appears to have increased with successive drafts of ICD-10. Clearly, agreement between the two major classification schemes is desirable. Indeed, ultimately, if progress is really being made, this should be reflected in greater concordance between classification schemes, as together they converge on 'the truth'. Unfortunately the reality is that convergence or divergence of views on classification often reflects the whim of fashion or the pressure of political persuasion. Inevitably psychiatrists, as researchers or as clinicians, need to be responsive to market forces (discharge diagnoses for hospital in-patients must conform to classification 'X', papers submitted to a certain journal will be frowned upon unless the authors use the official diagnostic scheme 'Y'). In recognising this, we must also recognise that our classifications remain but working hypotheses. It is always beneficial to redraft hypotheses in an attempt to improve clarity and precision. However, it is folly to indulge in redrafting for its own sake. We, therefore, suggest that the next decade should be one of consolidation and basic research. Carefully planned reliability studies, follow-up, and family studies need to be completed, but due consideration needs to be given also to aetiological factors. A genetic contribution to depression, particularly in its severer forms, is well established, and recent studies provide evidence of the heterogeneity of bipolar illness at the molecular level (see McGuffin, 1988). It is equally certain that environmental factors, including threatening and unpleasant events, have an important role in the aetiology of depression. But it must be remembered that the term 'environmental factors' encompasses certain forms of physical trauma as well as psychosocial adversity. The depressions are truly multifactorial in their aetiology, and progress beyond the stage of mere hypothesis requires acceptance of this complexity and a willingness to tackle it head on.

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References

American Psychiatric Association (1980) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn) (DSM-III). Washington, DC: APA.

—— (1987) *Diagnostic and Statistical Manual of Mental Disorders* (3rd end, revised) (DSM-III-R). Washington, DC: APA.

Andreasen, N. C., Scheftner, W., Reich, T., *et al* (1986) The validation of the concept of endogenous depression. *Archives of General Psychiatry*, **43**, 246–255.

Bebbington, P. E., Brugha, T., MacCarthy, B., *et al* (1988) The Camberwell Collaborative Depression Study: depressed probands: adversity and the form of depression. *British Journal of Psychiatry*, **152**, 754–765.

Blinder, M. G. (1966) The pragmatic classification of depression. *American Journal of Psychiatry*, **123**, 259–269.

Bridgman, P. W. (1927) *The Logic of Modern Physics*. New York: Macmillan.

Buchsbaum, M. S., Wu, J., Delisi, L. E., *et al* (1986) Frontal cortex and basal ganglia metabolic rates assessed by positron emission tomography with F-deoxyglucose in affective illness. *Journal of Affective Disorders*, **10**, 137–152.

Carney, M. W. P., Roth, M. & Garside, R. F. (1965) The diagnosis of depressive syndromes and the prediction of ECT response. *British Journal of Psychiatry*, **111**, 659–674.

Farmer, A. E., McGuffin, P. & Spitznagel, E. L. (1983) Heterogeneity in schizophrenia: a cluster analytic approach. *Psychiatry Research*, **8**, 1–12.

Feighner, J. P., Robins, E., Guze, S. B., *et al* (1972) Diagnostic criteria for use in psychiatric research. *Archives of General Psychiatry*, **26**, 57–67.

Foulds, G. A. & Bedford, A. (1975) Hierarchy of classes of personal illness. *Psychological Medicine*, **5**, 181–192.

Gershon, E. S., Hamovit, J., Guroff, J. J., *et al* (1982) A family study of schizoaffective bipolar I, bipolar II, unipolar and normal control probands. *Archives of General Psychiatry*, **39**, 1157–1167.

Halbreich, V., Grunhaus, L. & Ben-David, M. (1979) 24 hour rhythm of prolactin in depressive patients. *Archives of General Psychiatry*, **36**, 1183–1186.

Hempel, C. G. (1961) Introduction to problems of taxonomy. In *Field Studies in the Mental Disorders* (ed. J. Zubin). New York: Grune and Stratton.

Jablensky, A. (1988) Methodological issues in psychiatric classification. *British Journal of Psychiatry* (suppl. 1), **152**, 15–20.

Joyce, P. R., Sellman, J. D., Donald, R. A., *et al* (1988) The unipolar–bipolar depressive dichotomy of the relationship between afternoon prolactin and cortisol levels. *Journal of Affective Disorders*, **14**, 189–195.

Kafka, M. S., Nurnberger, J. I., Siever, L., *et al* (1986) 2 adrenergic receptor function in patients with unipolar and bipolar affective disorders. *Journal of Affective Disorders*, **10**, 163–169.

Katschnig, H. & Berner, P. (1983) The poly-diagnostic approach in psychiatric research. In *World Health Organization: Proceedings of the International Conference on Diagnosis and Classification of Mental Disorders and Alcohol and Drug Related Problems*. Geneva: WHO.

Kendell, R. E. (1975) *The Role of Diagnosis in Psychiatry*. Oxford: Blackwell Scientific Publications.

—— (1976) The classification of depressions: a review of contemporary confusion. *British Journal of Psychiatry*, **129**, 15–28.

Leonhard, K. (1959) *Aufteilung der Endogen Psychoses* (2nd edn). Berlin: Akademic Verlag.

Lewis, A. J. (1934) Melancholia: a clinical survey of depressive states. *Journal of Mental Science*, **80**, 277–378.

Linnoila, M., Whorton, A. R., Rubinon, D. R., *et al* (1983) C.S.F. prostaglandin levels in depressed and schizophrenic patients. *Archives of General Psychiatry*, **40**, 405–406.

McGuffin, P. (1988) Major genes for major affective disorder? *British Journal of Psychiatry*, **153**, 591–596.

——, Farmer, A. E., Gottesman, I. I., *et al* (1984) Twin concordance for operationally defined schizophrenia: confirmation of familiality and heritability. *Archives of General Psychiatry*, **41**, 541–545.

——, Katz, R., Aldrich, J., *et al* (1988*a*) The Camberwell Collaborative Depression Study: investigation of family members. *British Journal of Psychiatry*, **152**, 766–774.

——, —— & Bebbington, P. E. (1988*b*) The Camberwell Collaborative Depression Study: depression and adversity in the relatives of depressed probands. *British Journal of Psychiatry*, **152**, 775–782.

Muscettola, G., Potter, W. Z., Pickar, D., *et al* (1984) Urinary 3-methoxy-4-hydroxyphenyl-glycol plus major affective disorders. *Archives of General Psychiatry*, **41**, 337–342.

Parker, G., Kiloh, L. & Hayward, L. (1988) Parental representation of neurotic and endogenous depressives. *Journal of Affective Disorders*, **13**, 75–83.

Paykel, E. S. (1971) Classification of depressed patients: a cluster analysis derived grouping. *British Journal of Psychiatry*, **118**, 275–288.

Phelps, M. E., Mazziotta, J. C., Baxter, L., *et al* (1984) Positron emission tomographic study of affective disorders: problems and strategies. *Annals of Neurology* (suppl.), **15**, S149–S156.

Robins, E. & Guze, S. B. (1970) Establishment of diagnostic validity in psychiatric illness: its application to schizophrenia. *American Journal of Psychiatry*, **126**, 983–987.

ROY, A., PICKAR, D., LINNOILA, M., *et al* (1985) Plasma norepinephrine levels in affective disorders. *Archives of General Psychiatry*, 42, 1181–1185.

SARTORIUS, N. (1988) International perspectives of psychiatric classification. *British Journal of Psychiatry* (suppl. 2), 152, 9–14.

SPITZER, R. L., ENDICOTT, J. & ROBINS, E. (1975) *Research Diagnostic Criteria Instrument No. 58*. New York: New York State Psychiatric Institute.

STENGEL, E. (1959) Classification of mental disorders. *Bulletin of the WHO*, 21, 601–663.

TSUANG, M. T., FARAONE, S. V. & FLEMING, J. A. (1985) Familial transmission of major affective disorders. Is there evidence supporting the distinction between unipolar and bipolar disorders? *British Journal of Psychiatry*, 146, 268–274.

WING, J., COOPER, J. E. & SARTORIUS, N. (1974) *The Measurement and Classification of Psychiatric Symptoms*. London: Cambridge University Press.

—— & STURT, E. (1978) *The PSE–ID–CATEGO System. Supplementary Manual, Mimeograph*. London: MRC Social Psychiatry Unit, Institute of Psychiatry.

WOLFE, J., GRANHOLM, E., BUTTERS, N., *et al* (1987) Verbal memory deficits associated with major affective disorders: a comparison of unipolar and bipolar patients. *Journal of Affective Disorders*, 13, 83–92.

WORLD HEALTH ORGANIZATION (1974) *Glossary of Mental Disorders and Guide to their Classification for Use in Conjunction with the International Classification of Diseases, 8th Revision* (ICD–8). Geneva: WHO.

—— (1978) *Mental Disorders: Glossary and Guide to their Classification in Accordance with the 9th Revision of the International Classification of Diseases* (ICD–9). Geneva: WHO.

—— (1988) *International Classification of Diseases. 10th edition. Mental, Behavioral and Developmental Disorders*. Geneva: WHO.

YOUNG, M. A., SCHEFTNER, W. A., KLERMAN, G. L., *et al* (1986) The endogenous subtype of depression: a study of its internal contract validity. *British Journal of Psychiatry*, 148, 257–268.

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Computerised Tomography in Schizophrenia
Familial Versus Non-Familial Forms of Illness

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Findings on CT and demographical or clinical data in 80 patients with DSM-III schizophrenia and 45 medical controls were evaluated. Multiple-discriminant analysis showed that the enlargement of the third ventricle and frontal and parietal atrophy could significantly predict the diagnosis of schizophrenia. Widening of Sylvian fissures and parietal atrophy differentiated familial schizophrenics of both horizontal transmission (who had affected siblings) and vertical transmission (who had affected parents or/and offspring) from non-familial patients. Parietal atrophy and a history of birth complications differentiated horizontal from vertical transmission. The CT findings together with some clinical characteristics could differentiate the three subgroups classified by the hereditary form; thus each of these subgroup may belong to a different disease entity, of a different pathophysiology.

Subgrouping schizophrenic disorder based on defined biological markers is one of the most urgent topics of modern psychiatry. Computerised tomography (CT) studies on schizophrenia pioneered by Johnstone *et al* (1976) revealed that some patients with schizophrenia have neuromorphological abnormalities. These findings gave impetus to subgrouping schizophrenic disorder and to postulating the clinical characteristics of schizophrenics having abnormalities on CT, using neuropsychological testing, neurological soft signs, pre-morbid adjustment, treatment response, and positive/negative symptoms. The results of these studies seem equivocal. More reliable variables which are correlated with abnormalities on CT are biological markers, such as the genetic component or neurotransmission-related substances in cerebrospinal fluid (van Kammen *et al*, 1986; Reveley *et al*, 1987).

Some CT scan studies proposed that the size of the lateral ventricles is genetically controlled (Weinberger *et al*, 1981; Reveley *et al*, 1984*a*; Buchsbaum *et al*, 1984; DeLisi *et al*, 1986). The evidence that familial factors are of aetiological importance for schizophrenic disorder has prevailed since Kraepelin's suggestion (1913). Furthermore, a recent study has confirmed that schizophrenic illness according to DSM-III criteria (American Psychiatric Association, 1980) is a familial disorder (Kendeler *et al*, 1985), and Kendler & Hays (1982) have inferred the validity of the presence or absence of a family history of schizophrenia for subgrouping the disorder.

The present study was based on the hypothesis that schizophrenia could be classified according to the nature of family history; non-familial schizophrenia; familial schizophrenia with horizontal transmission (HT) (siblings also suffering from schizophrenia); familial schizophrenia with vertical transmission (VT) (schizophrenia in parents or/and offspring); and familial schizophrenia with mixed transmission (MT). We addressed the four following questions.

(a) What CT findings allow the diagnosis of schizophrenia as a whole?
(b) Do findings on CT differ according to the nature of the family history of schizophrenia?
(c) What is the nature of the CT findings, and are they progressive or stationary?
(d) Are there any relationships between positive or negative symptoms and findings on CT?

Method

Eighty patients who fulfilled DSM-III criteria for schizophrenic disorder and 45 control patients participated in this study. All subjects gave their informed consent, were Japanese, and were under 50 years old. The schizophrenic patients were all staying in hospital, and were all medicated with conventional neuroleptics at the time of the examination. Patients without a history of a psychiatric examination who consulted the internal medicine or neurosurgery department with such complaints as a headache, head injury, sensory problem, etc., and consequently showed no apparent pathological findings, served as controls. Subjects with a history of alcohol and/or drug abuse, and/or abnormal findings in the neurological examination were excluded.

The following demographic and clinical variables were documented in all of the schizophrenic patients: age at onset; duration of illness; number of hospital admissions; cumulative duration of hospital stays; a family history of DSM-III schizophrenia, diagnosed from the information collected from the patient's family and/or from the patient himself, and case notes. Patients who proved to have a family history of schizophrenia were divided into three groups, according to transmission (HT, VT, MT). Birth complications including premature birth, body weight under 2.5 kg, asphyxia, toxaemia of pregnancy, and artificial labour were also recorded.

Psychiatric interviews were performed as shortly as possible before the CT scan, and positive and negative symptoms were evaluated. Positive symptoms were scored according to Schneider's (1962) first-rank symptoms and negative symptoms were represented by the total scores of five items according to Andreasen *et al* (1982). Global response to neuroleptics was assessed retrospectively, and was scored 'excellent' when positive symptoms disappeared within three months, 'good' when partial improvement occurred, and 'failed' when no improvement occurred.

A GE CT/T 8800 × 2 scanner was used, with a 160 × 160 matrix, to take 10–12 cuts parallel to the orbitomeatal line at intervals of 10 mm. The magnification of the film was 0.4. During the evaluation of the CT findings, ventricle : brain ratio (VBR) and sub-objective observation methods were employed. The CT scans were magnified 5.5 times using a projector (Leitz, Prado Universal type 31) on an automatic planimeter analysing board (Kontron Mop-1) and a maximum ventricular and intracranial area was obtained. VBR was calculated according to a method reported by Synek & Reuben (1976). The lateral ventricles were analysed at a level at which the corpus appears in conjunction with their maximum areas, to give VBR_1. The maximum area of the third ventricle was analysed at a level at which the anterior horns of the lateral ventricles and superior colliculus appear, to give VBR_3. Cerebral sulci were evaluated at the levels at which the lateral ventricles appear, for the analysis of the atrophy of the frontal cortex; the widening of the interhemispheric fissure was evaluated at a level 30 mm higher than the cut in which the lateral ventricles appear the first time, for the analysis of the atrophy of the parietal cortex, and at the level at which the anterior horns appear, for the analysis of the enlargement of the Sylvian fissures. Enlargement of sulci or fissures was ranked on a scale of 0–3 for no, mild, moderate, and severe widening, as a whole on both sides and separately on each side. All CT scans were analysed randomly and blind, five times by one assessor, and mean values were taken. The intrarater reliability was 0.88 ($P<0.01$).

All data (means ± s.d.) were input into a microcomputer (PC 9801 VM), and treated by the two-tailed Student's *t*-test, Fisher's intraclass coefficient, and χ^2 analysis. Also, a multiple-regression analysis and multiple-discriminant analysis using the backward-elimination method or forward-entering method were utilised. Generally, the level of significance was set at 0.05, and at 0.1 for the multivariate analysis.

Results

Schizophrenics v. controls

In the controls, age significantly correlated with all CT findings except for the width of the interhemispheric fissure. Significant sex differences were seen for all CT findings in the controls.

Figures 1 and 2 represent the distribution of VBR_1 and VBR_3, respectively. As seen in Table I, all CT findings in schizophrenics significantly differed from those in controls. Since the sex ratio in the controls differed significantly from that of the schizophrenics, and the CT findings in the control samples varied with age and sex, corrections for the age and sex became necessary. A multiple-discriminant analysis showed that increased VBR_3, parietal atrophy, and frontal atrophy significantly predict the diagnosis of schizophrenia (Table II).

Familial v. non-familial schizophrenia

Widening of the Sylvian fissures and parietal atrophy significantly discriminated familial from non-familial patients (Table II). Familial schizophrenics with HT spent longer in hospital, had more negative symptoms, a greater VBR_1, and more enlarged Sylvian fissures as compared with non-familial ones (Table I). No significant differences in CT findings and clinical variables between familial schizophrenics with VT and non-familial patients were seen. A multiple-discriminant analysis revealed that parietal atrophy and a history of birth complications differentiated familial schizophrenics with HT from those with VT (Table II).

The nature of CT findings in schizophrenia

For evaluating CT findings in schizophrenia, it seems important to know whether the morphological changes are progressive or stationary. This problem could be partially answered by evaluating the correlation between duration of illness and CT scan changes. After correcting for age and sex, the duration of illness significantly correlated: with widening of the Sylvian fissures in the whole patient group (partial correlation coefficient, $r=0.19$, $P<0.1$); with frontal atrophy in non-familial subjects ($r=0.31$, $P<0.1$); negatively with VBR_1 ($r=-0.56$, $P<0.01$) and widening of the interhemispheric fissure ($r=-0.42$, $P<0.1$) in familial patients with HT; and positively with VBR_1 in familial patients with VT ($r=0.66$, $P<0.05$). The negative correlation between the duration of illness and VBR_1 in familial patients with HT could arise through the correlation of VBR_1 with age at onset in this subgroup ($r=0.55$, $P<0.05$).

Relationships between CT findings and clinical variables

Positive symptoms

In the whole group of schizophrenic patients, no CT findings predicted positive symptoms. In non-familial patients, widening of the Sylvian fissures (partial correlation coefficient, $r=0.37$, $P<0.05$), and less parietal atrophy ($r=-0.31$, $P<0.1$) were related to positive symptoms. In familial patients with HT, parietal atrophy ($r=0.54$, $P<0.05$) was related to positive symptoms. In familial patients with VT, a negative correlation between parietal atrophy and positive symptoms was seen ($r=-0.46$, $P<0.1$).

Negative symptoms

In the whole group and non-familial schizophrenic patients, frontal atrophy correlated with negative symptoms (partial

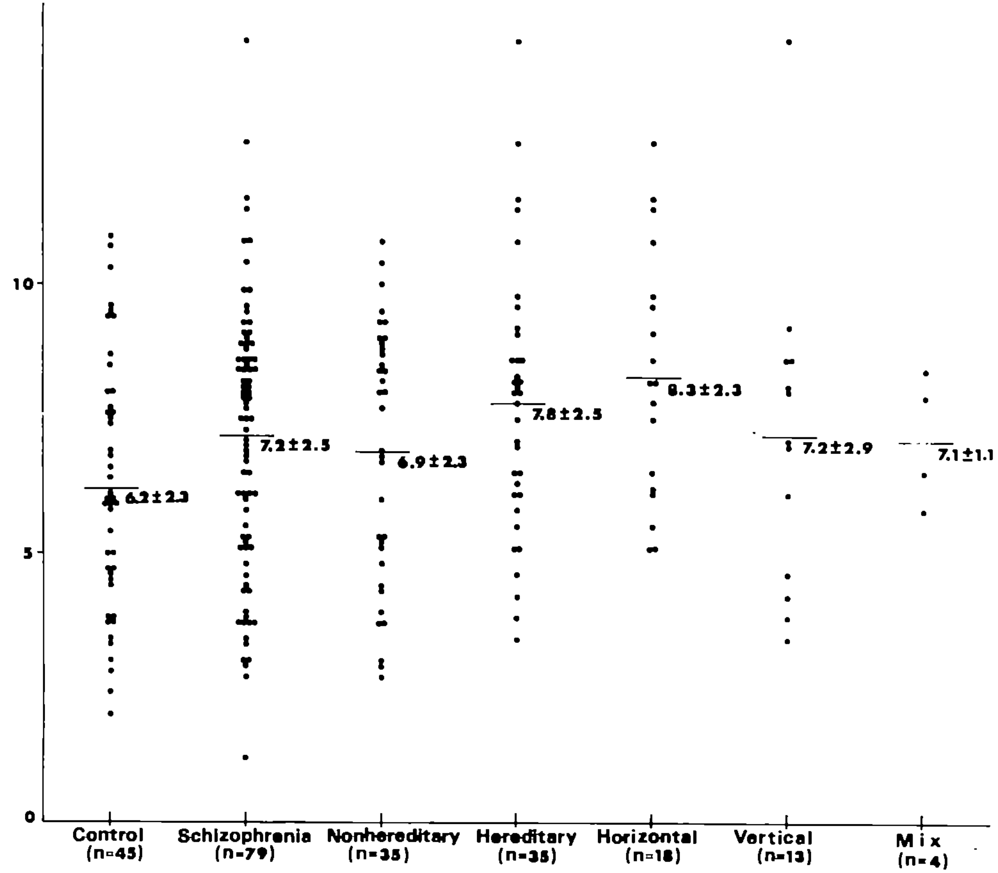

Fig. 1 The distribution of VBR$_1$ in each subgroup (a cut at which the corpus appears was not obtained in a case of schizophrenia).

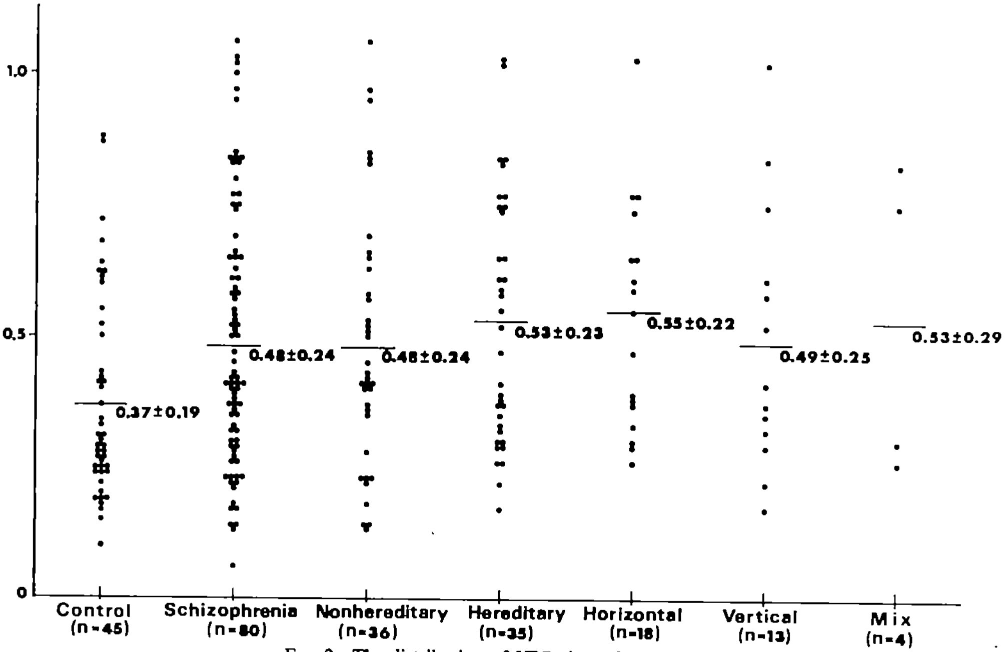

Fig. 2 The distribution of VBR$_3$ in each subgroup.

TABLE I

Clinical items and CT findings in each subgroup according to a hereditary form

	Controls	*Schizophrenics*					
	(n=45) (M/F, 16/29)	*(n=80) (M/F, 41/39)*	*Non-familial (n=36) (M/F, 15/21)*	*Familial (n=35) (M/F, 20/15)*	*Horizontal (n=18) (M/F, 12/6)*	*Vertical (n=13) (M/F, 6/7)*	*Mix (n=4) (M/F, 2/2)*
Age: years	34.6±10.3	32.1±8.3	31.0±9.0	34.1±7.6	34.2±6.9	32.9±5.1	37.0±5.3
Age at onset: years		23.4±6.6	22.9±7.5	24.1±5.5	23.7±4.7	23.0±6.1	30.0±5.5
Duration of illness: years		8.5±6.3	7.9±6.2	9.8±6.7	10.8±6.1	9.3±7.5	7.3±7.3
Duration of hospital stay: years		42.8±62.0	36.8±56.6	57.2±70.5	77.3±77.1***	39.4±66.6	30.8±31.0
Number of hospital admissions		2.2±1.5	2.1±1.5	2.3±1.5	2.2±1.3	2.4±1.7	2.5±1.9
Positive symptoms: Schneider score		2.4±1.6	2.6±1.5	2.1±1.7	2.3±2.0	2.2±1.2	1.3±1.5
Negative symptoms: Andreasen score		3.7±2.6	3.3±2.2	4.4±2.9	4.7±2.6***	3.8±3.3	5.0±2.7
VBR_1	6.28±2.39	7.21±2.50*	6.93±2.38	7.80±2.50	8.38±2.32***	7.2±2.96	7.19±1.17
VBR_3	0.38±0.19	0.49±0.24*	0.49±0.25	0.53±0.24	0.55±0.25	0.50±0.25	0.54±0.30
Widening of interhemispheric fissure[1]	1.07±0.50	1.44±0.63**	1.36±0.59	1.51±0.66	1.56±0.61	1.38±0.65	1.75±0.96
Frontal atrophy[1]	0.69±0.67	1.16±0.65**	1.08±0.55	1.25±0.74	1.28±0.83	1.15±0.68	1.50±0.58
left	0.67±0.71	1.13±0.66**	1.03±0.56	1.28±0.71	1.28±0.83	1.23±0.60	1.50±0.58
right	0.56±0.69	1.12±0.69**	0.97±0.61	1.29±0.75	1.27±0.82	1.23±0.73	1.50±0.58
Widening of sylvian fissures[1]	1.09±0.51	1.34±0.57*	1.17±0.51	1.54±0.61****	1.56±0.62***	1.46±0.66	1.75±0.50
left	1.09±0.51	1.39±0.65**	1.17±0.51	1.63±0.69****	1.72±0.67****	1.46±0.78	1.75±0.50
right	1.09±0.51	1.33±0.57*	1.19±0.52	1.46±0.61	1.61±0.70***	1.30±0.48	1.25±0.50
Parietal atrophy[1]	0.65±0.53	1.04±0.60**	1.03±0.42	1.17±0.73	1.35±0.86	0.85±0.55	1.00±0.00
left	0.65±0.53	0.99±0.63**	0.97±0.42	1.08±0.75	1.35±0.86	0.76±0.60	1.00±0.00
right	0.65±0.53	0.97±0.61**	0.97±0.50	1.03±0.72	1.29±0.85	0.69±0.48	1.00±0.00

1. Ranked on a scale of 0–3; 0 none, 1 mild, 2 moderate, 3 severe.

*$P<0.05$, **$P<0.01$ (comparison with control with Wilcoxon test or Student's *t*-test).

***$P<0.05$, ****$P<0.01$ (comparison with non-familial with Wilcoxon test or student's *t*-test).

TABLE II

Multiple-discriminant analyses for diagnosis and subgrouping

Dependent variable	*Group 1*	*Group 2*	*Wilks' Δ*	F
Independent variables	*Discriminant function*		*Partial F*	
Diagnosis	Control	Schizophrenia	0.7982	6.5715**
Age	0.3899	0.3308	4.9969*	
VBR$_3$	2.6537	4.7380	3.6857	
Parietal atrophy	−0.5205	0.4164	3.3417	
Frontal atrophy	0.0968	0.7981	2.4157	
Constant	−6.9818	−7.3540		
Family history	Non-familial	Familial	0.8191	2.6509
Widening of Sylvian fissure	1.4565	3.2031	6.0771*	
Parietal atrophy	4.8689	3.2455	3.5429	
Positive symptoms	1.5993	1.1855	2.3464	
Constant	−5.4385	−5.1742		
Family history	Vertical	Horizontal	0.7909	3.4379*
Parietal atrophy	1.1410	2.3786	5.1642*	
Birth complications	1.6324	0.1232	3.0961	
Constant	−0.9222	−1.6545		

Without asterisk, $P<0.1$, $^*P<0.05$, $^{**}P<0.001$.

correlation coefficient, $r=0.28$, $P<0.05$). In familial patients with HT, VBR$_1$ ($r=-0.59$, $P<0.05$) and widening of the interhemispheric fissure ($r=-0.47$, $P<0.05$) negatively correlated with negative symptoms. In familial patients with VT, VBR$_1$ ($r=0.66$, $P<0.05$) and parietal atrophy ($r=0.75$, $P<0.01$) were related to negative symptoms.

Response to neuroleptics

The subjects were divided into three groups according to the degree of response: 23 excellent; 51 good; and 6 did not respond. The 'excellent' group had a significantly shorter duration of illness (5.8 ± 4.9 v. 9.6 ± 6.5, $P<0.02$), and fewer negative symptoms (2.0 ± 1.2 v. 4.4 ± 2.7, $P<0.001$) compared with the others. Patients with a family history of schizophrenia in a first-degree relative responded to drugs no differently from those without such history. The 'excellent' respondents had less frontal atrophy than the others (0.87 ± 0.69 v. 1.28 ± 0.59, $P<0.01$).

Birth complications

The rate of occurrence of family histories in schizophrenics with birth complications (12/22) did not differ from that in patients without birth complications (23/49). VBR$_1$ was greater in schizophrenic patients without birth complications than in those with such a history (7.65 ± 2.37 v. 6.32 ± 2.57, $P<0.05$).

Discussion

CT findings in schizophrenics v. controls

VBR$_3$, parietal atrophy, and frontal atrophy were significant factors for diagnosing schizophrenic disorder (Table II). Enlargement of the lateral ventricles did not predict a diagnosis of schizophrenia, supporting previous studies (Largen *et al*, 1984; Pandurangi *et al*, 1984; Boronow *et al*, 1985; Shima *et al*, 1985). The importance of enlargement of the third ventricle as a change in schizophrenia also supports previous findings (Moriuchi, 1981; Gross *et al*, 1982; Dewan *et al*, 1983; Smith & Maser, 1983; DeMeyer *et al*, 1984; Takahashi *et al*, 1981; Pandurangi *et al*, 1984; Nasrallah *et al*, 1985).

Many CT studies of cerebral sulci in schizophrenics have been divided into those that suggest definite cerebral atrophy in schizophrenia (Rieder *et al*, 1979; Nasrallah *et al*, 1982; Largen *et al*, 1984; Oxenstierna *et al*, 1984; Smith *et al*, 1985) and those that suggest no such cerebral sulcal enlargement (Johnstone *et al*, 1976; Moriuchi, 1981; Okasha & Madkour, 1982; Gross *et al*, 1982; Pandurangi *et al*, 1984). The present study supports the importance of cerebral atrophy, especially, in the frontal and parietal region, in the diagnosis of schizophrenia.

Effects of the hereditary form on CT findings

Some authors have reported differences in cerebral atrophy (Oxenstierna *et al*, 1984) or VBR (Nasrallah *et al*, 1983*a*; Owens *et al*, 1985) between non-familial schizophrenics and familial ones. The evidence that discordant siblings (Weinberger *et al*, 1981) or discordant monozygotic twins (Reveley *et al*, 1982) had a larger VBR than healthy controls suggests a relationship between disposition for schizophrenia and enlargement of the lateral ventricles. On the other hand, two studies have shown that familial schizophrenic patients had small lateral ventricles (Buchsbaum *et al*, 1984; Reveley *et al*, 1984*b*). Some studies reported no differences in CT findings between familial and non-familial patients. However, these studies had rather small statistical bases (Farmer *et al*, 1985; Pearlson *et al*, 1985), or included other mental disorders in the family history (Campbell *et al*, 1979; Williams *et al*, 1985; Pearlson *et al*, 1985), or also extended the family history to second- or even third-degree relatives (Alm *et al*, 1984, Takahashi *et al*, 1981).

The present study demonstrated relationships between CT findings and clinical variables in the three hereditary subgroups.

(a) In non-familial patients, frontal atrophy appears to be a progressive change, because of the correlation with duration of illness, and is associated with negative symptoms. In this group, reverse correlation between positive symptoms and parietal atrophy was seen.

(b) In familial patients with HT, VBR$_1$ and widening of interhemispheric fissure correlated with age at onset, and consequently, negative correlations between these CT scan measures and duration of illness were seen. This means that patients with onset at a young age show small VBR_1. Interestingly, Buchsbaum *et al* (1984) reported uniformly small lateral ventricles in four monozygotic quadruplets concordant for schizophrenia. In this subgroup, VBR_1 and widening of the interhemispheric fissure were associated with severe negative symptoms, and positive symptoms correlated positively with parietal atrophy.

(c) In familial patients with VT, VBR_1 correlated with duration of illness and negative symptoms, and positive symptoms correlated negatively with parietal atrophy.

All these findings suggest that familial schizophrenia of HT is unique in terms of pathology and phenomenology.

CT findings and clinical variables

Although most studies of drug response and CT findings have proposed the importance of VBR (Weinberger *et al*, 1980; Jeste *et al*, 1982; Schulz *et al*, 1983; Luchins *et al*, 1984; Williams *et al*, 1985; Smith *et al*, 1985), a few studies have denied the relationship (Nasrallah *et al*, 1983*a*; Losonczy *et al*, 1986). Smith & Maser (1983) have demonstrated that schizophrenic patients with mild cortical atrophy showed the best clinical response, and patients with no cortical atrophy or severe cortical atrophy showed a poorer clinical response. On the contrary, Nasrallah *et al* (1983*b*) demonstrated that atrophy of the cerebral cortex was not related to the treatment effects of antipyschotic drugs. In the present study, excellent drug response was associated with less frontal atrophy, regardless of hereditary trait.

Previous studies have demonstrated a higher rate of history of birth complications in non-familial schizophrenics than in familial patients (Reveley *et al*, 1984*b*; Turner *et al*, 1986). The present study, however, does not confirm this. The method of sampling might contribute to the results of the present study, in which only in-patients, possibly severer cases, were examined.

Conclusions

CT findings and some clinical characteristics could differentiate familial from non-familial schizophrenia. Furthermore, the differentiation of three subgroups classified according to the hereditary form suggests that each might belong to a different disease entity based on a different pathophysiology. The CT findings in familial patients with HT seem to be inborn changes, because they correlated negatively with duration of illness. HT in schizophrenia may therefore carry a special significance. When considering the HT of schizophrenia, the retrovirus/transposon hypothesis proposed by Crow (1984) is highly interesting. He claimed that schizophrenia could be due to the integration of retrovirus into the human genome possibly through horizontal transmission at a critical developmental stage in a latent (proviral) form, to be expressed as a disease in adult life.

References

Alm, T., Lindstrom, L. H., Ost, L-G., *et al* (1984) Electrodermal non-responding in schizophrenia: relationships to attentional, clinical, biochemical, computed tomographical and genetic factors. *International Journal of Psychophysiology*, **1**, 195–208.

American Psychiatric Association (1980) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn) (DSM–III). Washington, DC: APA.

Andreasen, N. C., Olsen, S. A., Dennert, J. W., *et al* (1982) Ventricular enlargement in schizophrenia: relationship to positive and negative symptoms. *American Journal of Psychiatry*, **139**, 292–302.

Boronow, J., Pickar, D., Ninan, P. T., *et al* (1985) Atrophy limited to the third ventricle in chronic schizophrenic patients. *Archives of General Psychiatry*, **42**, 266–271.

Buchsbaum, M. S., Mirsky, A. F., Delisi, L. E., *et al* (1984) The genain quadruplets: electrophysiological, positron emission, and x-ray tomographic studies. *Psychiatry Research*, **13**, 95–108.

Campbell, R., Hays, P., Russell, D. B., *et al* (1979) CT scan variants and genetic heterogeneity in schizophrenia. *American Journal of Psychiatry*, **136**, 722–723.

Crow, T. J. (1984) A re-evaluation of the viral hypothesis: is psychosis the result of retroviral integration at a site close to the cerebral dominance gene? *British Journal of Psychiatry*, **145**, 234–253.

Delisi, L. E., Goldin, L. R., Hamovit, J. R., *et al* (1986) A family study of the association of increased ventricular size with schizophrenia. *Archives of General Psychiatry*, **43**, 148–153.

Demeyer, M. K., Gilmor, R., Demeyer, W. E., *et al* (1984) Third ventricle size and ventricular/brain ratio in treatment-resistant psychiatric patients. *Journal of Operational Psychiatry*, **15**, 2–8.

Dewan, M. J., Pandurangi, A. K., Lee, S. H., *et al* (1983) Central brain morphology in chronic schizophrenic patients: a controlled CT study. *Biological Psychiatry*, **18**, 1133–1140.

Farmer, A., McGuffin, P., Jackson, R., *et al* (1985) Classifying schizophrenia. *Lancet*, *i*, 1333.

Gross, G., Huber, G. & Schuttler, R. (1982) Computerized tomography studies on schizophrenic diseases. *Archive für Psychiatrie und Nervenkrankheiten*, **231**, 519–526.

Jeste, D.V., Kleinman, J. E., Potkin, S. G., *et al* (1982) Ex uno multi: Subtyping the schizophrenic syndrome. *Biological Psychiatry*, **17**, 199–222.

Johnstone, E. C., Crow, T. J., Frith, C. D., *et al* (1976) Cerebral ventricular size and cognitive impairment in chronic schizophrenia. *Lancet*, *i*, 924–926.

Kendler, K. S. & Hays, P. (1982) Familial and sporadic schizophrenia: a symptomatic, prognostic, and EEG comparison. *American Journal of Psychiatry*, **139**, 1557–1562.

——, Gruenberg, A. M. & Tsuang, M. T. (1985) Psychiatric illness in first-degree relatives of schizophrenic and surgical control patients. *Archives of General Psychiatry*, **42**, 770–779.

Kraepelin, E. (1913) *Psychiatrie. Achte vollstandig umgearbeitete Auflage. III. Band. Klinische Psychiatrie. II. Teil.* Leipzig: Johann Ambrosius Barth.

Largen, J. W., Jr, Smith, R. C., Calderon, M., *et al* (1984) Abnormalities of brain structure and density in schizophrenia. *Biological Psychiatry*, **19**, 991–1013.

Losonczy, M. F., Song, I. S., Mohs, R. C., *et al* (1986) Correlates of lateral ventricular size in chronic schizophrenia. I. Behavioral and treatment response measures. *American Journal of Psychiatry*, **143**, 976–981.

Luchins, D. J., Lewine, R. R. J. & Meltzer, H. Y. (1984) Lateral ventricular size, psychopathology, and medication response in the psychoses. *Biological Psychiatry*, **19**, 29–44.

Moriuchi, I. (1981) A study of schizophrenic brains by computerized tomography scans. *Folia Psychiatrica et Neurologica Japonica*, **35**, 55–72.

Nasrallah, H. A., McCalley-Whitters, M. & Jacoby, C. G. (1982) Cortical atrophy in schizophrenia and mania: a comparative CT study. *Journal of Clinical Psychiatry*, **43**, 439–441.

——, Kuperman, S., Hamra, B. J., *et al* (1983*a*) Clinical differences between schizophrenic patients with and without large cerebral ventricles. *Journal of Clinical Psychiatry*, **44**, 407–409.

——, ——, Jacoby, C. G., *et al* (1983*b*) Clinical correlates of sulcal widening in chronic schizophrenia. *Psychiatry Research*, **10**, 237–242.

——, Jacoby, C. G., Chapman, S., *et al* (1985) Third ventricular enlargement on CT scans in schizophrenia: association with cerebellar atrophy. *Biological Psychiatry*, **20**, 443–450.

Okasha, A. & Madkour, O. (1982) Cortical and central atrophy in chronic schizophrenia. *Acta Psychiatrica Scandinavica*, **65**, 29–34.

Oxenstierna, G., Bergstrand, G., Bjerkenstedt, L., *et al* (1984) Evidence of disturbed CSF circulation and brain atrophy in cases of schizophrenic psychosis. *British Journal of Psychiatry*, **144**, 654–661.

Owens, D. G. C., Johnstone, E. C., Crow, T. J., *et al* (1985) Lateral ventricular size in schizophrenia: relationship to the disease process and its clinical manifestations. *Psychological Medicine*, **15**, 27–41.

Pandurangi, A. K., Dewan, M. J., Lee, S. H., *et al* (1984) The ventricular system in chronic schizophrenic patients. A controlled computed tomography study. *British Journal of Psychiatry*, **144**, 172–176.

Pearlson, G. D., Garbacz, D. J., Moberg, P. J., *et al* (1985) Symptomatic, familial, perinatal, and social correlates of computerized axial tomography (CAT) changes in schizophrenics and bipolars. *Journal of Nervous and Mental Disease*, **173**, 42–50.

Reveley, A. M., Reveley, M. A., Clifford, C. A., *et al* (1982) Cerebral ventricular size in twins discordant for schizophrenia. *Lancet*, *i*, 540–541.

——, ——, Chitkara, B., *et al* (1984*a*) The genetic basis of cerebral venticular volume. *Psychiatry Research*, **13**, 261–266.

——, —— & Murray, R. M. (1984*b*) Cerebral ventricular enlargement in non-genetic schizophrenia: a controlled twin study. *British Journal of Psychiatry*, **144**, 89–93.

——, Belleroche, J. D., Recordati, A., *et al* (1987) Increased CSF amino acids and ventricular enlargement in schizophrenia: a preliminary study. *Biological Psychiatry*, **22**, 413–420.

Rieder, R. O., Donnelly, E. F., Herdt, J. R., *et al* (1979) Sulcal prominence in young chronic schizophrenic patients: CT scan findings associated with impairment on neuropsychological tests. *Psychiatry Research*, **1**, 1–8.

Schneider, K. (1962) *Klinische Psychopathologie*. Stuttgart: Georg Thieme.

Schulz, S. C., Sinicrope, P., Kishore, P., *et al* (1983) Treatment response and ventricular brain enlargement in young schizophrenic patients. *Psychopharmacology Bulletin*, **19**, 510–512.

Shima, S., Kanba, S., Masuda, Y., *et al* (1985) Normal ventricles in chronic schizophrenics. *Acta Psychiatrica Scandinavica*, **71**, 25–29.

Smith, R. C. & Maser, J. (1983) Morphological and neuropsychological abnormalities as predictors of clinical response to psychotrophic drugs. *Psychopharmacology Bulletin*, **19**, 505–509.

——, Baumgartner, R., Ravichandran, G. K., *et al* (1985) Lateral ventricular enlargement and clinical response in schizophrenia. *Psychiatry Research*, **14**, 241–253.

Synek, V. & Reuben, J. R. (1976) The ventricular-brain ratio using planimetric measurement of EMI scans. *British Journal of Radiology*, **49**, 233–237.

Takahashi, R., Inaba, Y., Inanaga, K., *et al* (1981) CT scanning and the investigation of schizophrenia. In *Biological Psychiatry 1981* (eds C. Perris, G. Struwe & B. Jansson). Amsterdam. Elsevier/North-Holland Biomedical Press.

Turner, S. W., Toone, B. & Brett-Jones, J. R. (1986) Computerized tomographic scan changes in early schizophrenia-preliminary findings. *Psychological Medicine*, **16**, 219–225.

van Kammen, D. P., van Kammen, W. B., Mann, L. S., *et al* (1986) Dopamine metabolism in the cerebrospinal fluid of drug-free schizophrenic patients with and without cortical atrophy. *Archives of General Psychiatry*, **43**, 978–983.

Weinberger, D. R., Bigelow, L. B., Kleinman, J. E., *et al* (1980) Cerebral ventricular enlargement in chronic schizophrenia. *Archives of General Psychiatry*, **37**, 11–13.

——, DeLisi, L. E., Neophytides, A. N., *et al* (1981) Familial aspects of CT scan abnormalities in chronic schizophrenic patients. *Psychiatry Research*, **4**, 65–71.

Williams, A. O., Reveley, M. A., Kolakowska, T., *et al* (1985) Schizophrenia with good and poor outcome. II: Cerebral ventricular size and its clinical significance. *British Journal of Psychiatry*, **146**, 229–246.

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Prospects of Rehabilitation for Elderly Schizophrenics

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The psychopathology and disabilities of a group of institutionalised elderly schizophrenics were compared with those of a group of non-schizophrenic elderly, and with younger schizophrenics reported in a parallel study and in the literature. Elderly schizophrenics showed significantly more psychopathology and disability than the non-schizophrenic elderly; however, they exhibited less psychopathology than younger schizophrenics. Disability among elderly schizophrenics was not correlated with chronicity of institutionalisation or psychopathology. There was a suggestion that disability among elderly schizophrenics may be due to organic deterioration.

The plight of elderly schizophrenics has traditionally been thought to be dismal. Even in this era of deinstitutionalisation, the belief persists that these patients will probably remain in hospital until death, despite data suggesting that schizophrenic symptoms decrease with age (Bridges *et al*, 1978; Dvorin, 1977), and that the negative features of schizophrenia, although more frequent in older schizophrenics (Ciompi, 1987), may actually be reversible in this population (Johnstone *et al*, 1987). Indeed, Ciompi (1987) found 27% complete remissions in elderly schizophrenics over 5 years, a considerable improvement in 'productive' symptomatology in two-thirds, and the presence of severe 'non-productive' symptomatology in only 18%. Institutionalisation may, therefore, not be maintained primarily by the illness-related factors, severity of illness and length of hospital stay (Goodman & Siegel, 1986). Other factors relevant to the poor prognosis of the elderly schizophrenic include chronic use of medication, with its immediate and long-term effects, multisystem disease, poor nutritional status, diminished overall strength and impaired mental functioning (Jarwick & Pere, 1981; Feldman, 1983). Another is the effect of chronic institutionalisation on self-care, social skills and vocational and family functioning (Wing & Brown, 1970; Anthony & Liberman, 1986). Finally, the attitude of ageism, viewing the elderly patient as a worthless, irretrievable, end-stage human being, which is often reflected in the family, caretakers and society, may play a major role (Blaschke, 1981).

What are the implications of the above in considering rehabilitation prospects for elderly institutionalised schizophrenics? Disabilities such as poor social skills and decreased ability for independent functioning, along with deteriorating medical status and age discrimination, may be related to the chronicity of institutionalisation or they may be a reflection of negative schizophrenic symptoms. Data on these disabilities in schizophrenics in general, and on their relationship to institutionalisation and the disease itself, have been extensively reported (Anthony & Liberman, 1986), but no studies could be found in the last ten years that directly dealt with the disabilities of elderly schizophrenics, or that compared the disability of an elderly institutionalised schizophrenic population with that of a non-schizophrenic population of elderly living in the community. In the present study, we assessed the psychopathology and disabilities of elderly institutionalised schizophrenics and compared them with those of a non-schizophrenic elderly population. It was expected that the schizophrenic population would show significantly more psychopathology than the non-schizophrenic population, but less than younger schizophrenics. It was also expected that the schizophrenics would show more disabilities than the non-schizophrenics; these disabilities were expected to be more strongly correlated with measures of institutionalisation than with measures of active schizophrenic symptoms.

Method

Subjects

Two groups of subjects participated in the present study.

Group A consisted of all ($n = 40$) the elderly, aged 65 and older, institutionalised chronic schizophrenics in six pavilions of the Dromokaition Mental Hospital in Athens. The diagnosis of schizophrenia was based on DSM–III criteria. The average age of these patients was 70.8 years, the average age at onset of schizophrenia was 27.3 years, the average number of years since onset was 43.3, and the average length of continuous stay in hospital was 29.2 years (range 3–44). All these patients had been receiving stable pharmacotherapy for at least one year. Current medications included antipsychotics (in 100%), anticholinergics (80%)

TABLE I
Demographic data for group of elderly schizophrenics (n = 40)[1]

Characteristic	*Distribution: %*
Sex	
Male	47.5
Female	52.5
Marital status	
Partner	15.0
No partner	85.0
Education	
0–6 years	57.5
7–18 years	42.5
Place of birth	
Urban	42.5
Rural	57.5
Economic status	
No support	55.0
Pension	45.0

[1] Distributions are the same in the matched group of day-care centre attenders.

and antidepressants (10%). Of these patients, 50% suffered from chronic medical diseases such as diabetes, hypertension, heart disease and other diseases.

Group B consisted of 40 elderly people attending adult day-care centres in Athens, who had not been diagnosed as suffering from psychiatric disorders. Individuals in this group were matched one-to-one to individuals in group A for age (within 2 years: mean = 70.8 years), sex, education and economic and marital (partner/no partner) status. Of this group, 35% suffered from chronic medical diseases.

The demographic data are shown in Table I.

Measures

Two measures were used, the Present State Examination (PSE), and the Blessed *et al* (1968) scales, both of which were administered by appropriately trained physicians, as follows.

The Present State Examination (PSE) (Wing *et al*, 1974) was shown by Murphy (1982, 1983) not to be age specific and to facilitate comparison between age groups. The PSE was used as a measure of current psychopathology for between-group comparison and for comparisons between mental state and disability.

Scales assessing changes in performance of everyday activities, in habits and in personality, interests and drives were adapted and translated into Greek from Blessed *et al* (1968). They were completed by nursing staff as informants in the case of group A and relatives for group B. These will be referred to as disability scales and were used to assess the functional and social capabilities of the two groups.

Analysis

First, the CATEGO program was used to obtain total PSE scores, scores on the PSE neurotic and psychotic subscales, prevalence of cases according to the CATEGO index of definition (ID), and prevalence of CATEGO classes and ICD–9 diagnoses. Scores were compared by Wilcoxon's test and categories by McNemar's test.

TABLE II
Prevalence of the various levels of Catego index of definition in each group

ID	*Group A: %*	*Group B: %*
1–4 (non-case)	12.5	70.0
5 (threshold)	32.5	17.5
6–8 (case)	55.0	12.5

Next, the disability scales for the two groups were compared for total score (as described by the scales' authors), and for the frequency with which every disability occurred in each group (by McNemar's test).

Finally, the Kruskal–Wallis test was used to compare total scores on the disability scales with the CATEGO 'caseness' on three levels (not a case, threshold, case), for each group separately. Spearman rank correlations were used to compare scores on the total PSE and its subscales with total disability scale scores for each group separately. Similar correlations were used to compare disability scores with age for both groups, and with years since onset of schizophrenia and length of stay in hospital for group A only.

Results

Present State Examination results

The PSE data arising from the present study have been discussed in detail elsewhere (Lyketsos *et al*, 1988). Briefly, comparison between the two groups for total PSE scores showed a significantly higher mean score for group A (17.3 v. 6.7, $P<0.0001$). The difference persisted for the scores on the two psychosis subscales of the PSE: on the delusions and hallucinations (DAH) subscale, group A scored 4.6 to group B's 0.1; on the behaviour, speech and other (BSO) subscale the scores were 9.8 and 0.1 respectively; for both, $P<0.0001$. However, on both neurosis subscales, group B scored significantly higher than group A: 2.5 v. 0.9 for the specific syndromes (SNR), and 4.0 v. 2.1 for the non-specific syndromes (NSN); for both, $P<0.006$.

With respect to ID 'caseness', there were many more threshold and definite cases in group A than in group B (Table II). Just over half of group A were defined as cases, while just over two-thirds of group B were defined as not being cases. As expected, most cases and threshold cases in group A received a CATEGO or ICD–9 diagnosis of one of the psychoses (97%), while in group B most cases and threshold cases received a diagnosis in one of the neurotic categories (92%).

It has been reported elsewhere (Lyketsos *et al*, 1988) that the psychopathology exhibited by group A on the PSE, in terms of total and subscale scores and in terms of prevalence

TABLE III

Spearman rank order correlations of PSE and total disability scores

	Group A		Group B	
	r	P	r	P
BSO	−0.13	0.42	+0.28	0.08
DAH	−0.06	0.72	+0.32	0.05
SNR	+0.04	0.81	+0.45	0.003
NSN	+0.04	0.83	+0.47	0.002
PSE (total)	−0.12	0.47	+0.51	0.001

TABLE IV

Spearman rank correlations between total disability scores and age, length of schizophrenic illness and stay in hospital

	Group A		Group B	
	r	P	r	P
Age	0.35	0.025	0.41	0.002
Length of stay in hospital	0.07	0.68	—	—
Length of illness	0.24	0.14	—	—

of cases and threshold cases, is significantly less than the psychopathology exhibited by a group of young institutionalised schizophrenics (mean age = 44) interviewed at the same hospital at the same time. This was also true when group A data were compared with data generated by the International Pilot Study for Schizophrenia (IPSS) for young schizophrenics (Lyketsos *et al*, 1988).

Analysis of disability measures

The total score on the disability measures was markedly higher in group A, with a median score of 11 (the highest was 28), compared with a median of 0.5 in group B ($P<0.0001$) by sign test). Of group B, 40% had a score of zero, compared with only 2.5% of group A.

Detailed comparison showed that of 22 disabilities assessed by these measures, 18 were significantly more prevalent among group A patients. Four disabilities were present in over two-thirds of group A patients but in less than 10% of group B subjects. These were: inability to perform household tasks; impairment of regard for feelings of others; diminished emotional responsiveness; and diminished initiative or growing apathy. The four disabilities not differing significantly in prevalence between groups were: inability to recall recent events; tendency to dwell in the past; sexual misdemeanour; and purposeless hyperactivity. No disability was more prevalent in group B.

Comparison of measures of disability and psychopathology

Comparison of CATEGO 'caseness' with total disability scores showed no significant variation in these scores across non-case, threshold and case IDs in group A ($\chi^2=1.92$, $P=0.38$). In contrast, total disability scores for group B were significantly higher for cases compared with non-cases and thresholds ($\chi^2=8.71$, $P=0.013$).

Table III shows the results of the Spearman rank order correlation analysis of scores on the total PSE, and its four subscales, with the total disability scores for each group separately.

There was no significant correlation between PSE scores and total disability scores for group A. For group B, however, this correlation approached significance at the 5% level for BSO scores, was significant for DAH scores, and highly significant for scores on the neurotic scales and the total PSE.

Finally, Table IV shows the correlation of total disability scores with age, length of schizophrenic illness and length of stay in hospital.

In both groups there was a significant correlation between age and degree of disability. However, in group A there was no correlation between disability and length of illness or stay in hospital.

Discussion

As expected, the PSE results showed a greater degree of psychopathology to be present in elderly institutionalised schizophrenics in comparison with elderly non-schizophrenics, with the exception of neurotic syndromes. However, as noted, this psychopathology was significantly less than that exhibited by younger schizophrenics both in a parallel study and in the published literature (WHO, 1973). This confirms the consistent finding in the literature that active schizophrenic symptomatology 'burns out' with age. These data offer an additional point of interest: an apparent decrease in negative schizophrenic symptoms with age as reflected in lower behaviour, speech and other psychotic features scores. However, despite this relative improvement of most features of schizophrenia, elderly schizophrenics exhibited a substantial number of psychotic disturbances and were more likely than not to be designated as cases by the PSE.

The disabilities of the elderly schizophrenic population were marked in comparison with those of the non-schizophrenic elderly. Their most severe disabilities were in the areas very likely affected by the negative symptoms of the illness, such as affect and motivation. Their ability to perform basic functions necessary to independent living, such as getting around, eating, dressing, shopping and handling money, was also severely impaired. However, functions such as memory seemed to be relatively preserved, although our measures were not accurate assessors of these functions. Unfortunately, the present study lacked a control group of younger schizophrenics to compare performance on these disability measures directly. Historical controls suggest that younger schizophrenics, when not in acute exacerbation of the illness, are generally much less disabled in such basic functions as are measured here and are often quite responsive to learning living and social skills (Harding & Brooks, 1984; Liberman *et al*, 1984; Wallace & Liberman, 1985).

What are the substantial disabilities exhibited by elderly schizophrenics most likely to be due to? The lack of correlation between the disabilities and degree of psychopathology in elderly schizophrenics, and the apparently much lower prevalence of the disabilities in younger schizophrenics, suggest that the disabilities may not so much reflect the schizophrenic illness as reflect the presence of institutionalisation and the chronicity of a debilitating mental illness. The absence of a correlation between disability and either length of illness or length of stay in hospital does not support this conclusion. However, the correlation may be falsely absent because of a ceiling effect that is repeatedly pointed out by many clinicians. That is, the disability produced by institutionalisation and chronic mental illness develops to its greatest degree relatively early in the course of the illness, so that beyond a certain point disability is so severe that it no longer worsens significantly.

It cannot be ruled out that the high degree of disability in elderly schizophrenics is a result of organic deterioration. Reports have appeared in the literature suggesting that schizophrenics are more frequently prone to such deterioration, and that this is most likely a process independent of the schizophrenic illness (Ciompi, 1987). The present study is somewhat supportive of such a view, since measures of disability tended to indicate worsening with advancing age in both the schizophrenic and the non-schizophrenic elderly.

How can we interpret these data in considering the rehabilitation of elderly schizophrenics? It appears that the main handicaps of elderly, institutionalised schizophrenics are disabilities in social and living skills, and only to a lesser degree the effects of their mental illness and its treatment. It is encouraging to believe that these disabilities may be subject to improvement through appropriate social skills training and support, as is the case with younger schizophrenics (Anthony & Liberman, 1986). The extent to which such an improvement can be brought about, in view of the chronicity of the disabilities and of the possible contribution of organic deterioration to their presence, remains an open question since, at present, no rehabilitation programmes are available locally for schizophrenics of any age. The evidence of the study suggests that the planning of such programmes should not ignore the claims of the elderly.

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References

Anthony, A. W. & Liberman, R. P. (1986) The practice of psychiatric rehabilitation: historical, conceptual and research base. *Schizophrenia Bulletin*, **12**, 542–547.

Blaschke, T. (1981) Potential drug interactions in aging patients. In *Age and the Pharmacology of Psychoactive Drugs* (ed. A. A. Ruskin). New York: Elsevier.

Blessed, G., Tomlinson, B. E. & Roth, M. (1968) The association between quantitative measures of dementia and of senile change in the cerebral grey matter of elderly subjects. *British Journal of Psychiatry*, **114**, 797–811.

Bridges, T. P., Cannon, E. & Wyatt, R. J. (1978) Burnt-out schizophrenia: evidence for age effects on schizophrenic symptomatology. *Journal of Gerontology*, **33**, 835–839.

Ciompi, L. (1987) Aging and schizophrenic psychosis. *Acta Psychiatrica Scandinavica*, **71**, Supplement 319, 93–97.

Dvorin, D. V. (1977) Patients with paranoid schizophrenia continuing into old age. *Zhurnal Nevropatologii i Psikhiatrii Imeni S. S. Korsakova*, *77*, 881–886.

Feldman, E. B. (1983) *Nutrition in the Middle and Later Years*. Boston: John Wright PSG.

Goodman, A. B. & Siegel, C. (1986) Elderly schizophrenic inpatients in the wake of deinstitutionalization. *American Journal of Psychiatry*, **143**, 204–207.

Harding, C. M. & Brooks, G. W. (1984) Life assessment of a cohort of chronic schizophrenics discharged 20 years ago. In *The Handbook of Longitudinal Research* (eds I. S. Mednick, S. M. Harway & K. Finello). New York: Praeger Press.

Jarwick, L. S. & Pere, M. (1981) Overview of physiologic dysfunction related to psychiatric problems in the elderly. In *Neuropsychiatric Manifestations of the Elderly* (eds A. J. Levinson & R. C. W. Hall). New York: Raven Press.

Johnstone, E. C., Owens, D. C. G., Frith, C. D., *et al* (1987) Relative stability of positive and negative features in chronic schizophrenia. *British Journal of Psychiatry*, **150**, 60–64.

Liberman, R. P., Falloon, I. R. H. & Wallace, C. J. (1984) Drug–psychosocial interventions in the treatment of schizophrenia. In *The Chronically Mentally Ill: Research and Services* (ed. M. Mirabi). New York: SP Medical and Scientific Books.

Lyketsos, G. C., Richardson, S. C., Mouzakis, D., *et al* (1988) Depressive syndromes and symptoms in elderly schizophrenics. *Experimental and Clinical Psychiatry*, **1**, 17–23.

Murphy, E. (1982) The social origins of depression in old age. *British Journal of Psychiatry*, **141**, 135–142.

Murphy, E. (1983) The prognosis of depression in old age. *British Journal of Psychiatry*, **142**, 111–119.

Wallace, C. J. & Liberman, R. P. (1985) Social skills training for patients with schizophrenia: a controlled clinical trial. *Psychiatry Research*, **15**, 239–243.

Wing, J. K. & Brown, J. (1970) *Institutionalism and Schizophrenia*. London: Cambridge University Press.

Wing, J. K., Cooper, J. E. & Sartorius, N. (1974) *The Measurement and Classification of Psychiatric Symptoms*. London: Cambridge University Press.

World Health Organization (1973) *The International Pilot Study on Schizophrenia*. Geneva: WHO Publications.

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Disturbed Endocrine Function in the Psychoses

I: Disordered Homeostasis or Disease Process?

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Plasma concentrations of prolactin, growth hormone, cortisol, TSH, and the neurophysins were measured over 17 hours in 98 newly admitted psychiatric patients and 35 control subjects. Seventy patients had been free of psychotropic medication for three months. Patients with schizoaffective mania (SAM) differed significantly from control subjects by increased plasma cortisol concentrations and decreased night-time TSH concentrations. The latter were also significantly lower than in both schizophrenic and manic disorder patients. Plasma cortisol was increased to a lesser extent in other psychotic subgroups, and increases in prolactin were most marked in the affective psychoses. There was little diagnostic specificity for psychoses other than SAM. Higher cortisol and prolactin levels may be due to the stimulatory effect of serotonergic pathways, but the neural mechanisms underlying lower night-time TSH levels in SAM are not known. The findings are not consistent with the view (a) that the hormonal changes of the psychoses simply reflect a non-specific response to stress, or (b) that the biological abnormalities of the psychoses can be accounted for by a single continuum of disturbance.

The most commonly described biological model of the psychoses assumes discrete disease entities, each with characteristic symptoms and signs arising from separate aetiologies. This view is supported by the distinctions that can be made between psychoses using, for example, family history data (Tsuang *et al*, 1980) or response to treatment (Taylor *et al*, 1974). In the absence of consistent neuropathological changes, the most plausible biological model of the psychoses implicates abnormalities in central neurotransmission, such as dopamine in schizophrenia (Snyder *et al*, 1974), and noradrenaline or serotonin in depressive illness (Charney *et al*, 1981). Much current biological research in psychiatry is, therefore, directed towards identifying the particular neurotransmitter disturbance that best explains the onset of each type of disorder and the mode of action of effective treatments.

One potentially informative approach is to test the hypothesis that the simultaneous investigation of many variables, each regulated by those neurotransmitters implicated in the psychoses, will separate a diagnostically heterogeneous population into groups characterised by specific clinical features. Multivariate analysis of this type has been widely used in psychopathological and socio-demographic studies in psychiatry, but, with few exceptions (e.g. Shagass *et al*, 1985), has been little used in biological research. If the approach was successful, the biological data would provide an important addition to the already extensive clinical criteria that distinguish between subtypes of psychoses, and might later be developed into rapid and reliable diagnostic tests (Kendell, 1982).

The secretion of pituitary hormones is regulated by the same neurotransmitters likely to be involved in the aetiology of the psychoses. We have tested the specific hypothesis that the measurement of plasma hormones over an extended (17-hour) sampling period would separate a diagnostically heterogeneous patient sample into groups that would correspond with the classification of the same sample using Research Diagnostic Criteria (RDC; Spitzer *et al*, 1978). Previously, our psychoneuroendocrine studies have shown that in young men with mania, there is a selective increase in concentrations of plasma lutenising hormone (Whalley *et al*, 1985, 1987*a*, 1987*b*), that plasma cortisol was increased in many psychotic patients (Christie *et al*, 1986), and that there are characteristic hormonal changes in Alzheimer's disease (Christie *et al*, 1987).

We now report plasma concentrations of cortisol, growth hormone (GH), prolactin (PRL), thyroid-stimulating hormone (TSH), and oestrogen-stimulated neurophysin (ESN) in carefully diagnosed, drug-free psychotic patients. Plasma neurophysins were measured in preference to oxytocin and vasopressin because the neurophysins provide a more accurate index of their overall secretion. We know of no other study where all these pituitary hormones have been examined in the same patients.

The statistical analysis of these data presents several problems, partly because of the number of variables studied at several time points, and partly because of the number of groups. Firstly, we wished to determine whether hormonal data distinguished between diagnostic groups. Many hormones vary substantially by sex, age, and reproductive status, and so we excluded the gonadotrophins and reported these separately (Whalley *et al*, 1985). Multivariate statistical techniques can demonstrate overall differences between groups, and make appropriate adjustments for the effects of time, age, and sex. This approach represents the most satisfactory resolution of the conceptual and statistical problems arising during testing of the study hypothesis. Secondly, we wished to locate differences, where these existed, between diagnostic groups, and sought to do this by univariate one-way analysis of variance, corrected for the number of tests performed. Thirdly, we wished to classify systematically the complex endocrine data, using discriminant function analysis, and to compare the classification obtained with the categorisation of patients using RDC (see Whalley *et al*, 1989 – this issue, pp. 462–467).

Method

Subjects

Ninety-eight patients routinely admitted to hospital and 35 control subjects were studied. The sample contained 5–10% of acute psychotic patients admitted to the Royal Edinburgh Hospital during the study period, and was drawn from a larger sample of 137 newly admitted patients, of whom 39 were later removed for a history of endocrine, renal or liver disease, intercurrent physical illness, drug or alcohol addiction, or for taking oral contraceptives within 12 weeks. All patients understood that the research procedures were unrelated to their treatment, and gave their informed consent. In cases of doubt, only when both a relative and patient agreed was that patient included. The Present State Examination (PSE; Wing *et al*, 1974), completed within two weeks of admission, was assessed with the clinical history independently by two psychiatrists (JEC and LJW) six months after discharge, when patients were classified according to RDC, without knowledge of the results of the endocrine investigations. In three cases where raters disagreed, a third rater (IMB) arbitrated. The classification was, therefore, based on a standardised mental state (the PSE), and routine clinical observations, and allowance was made for any new information (for example, a previously concealed history of illicit drug use excluded one patient). There was good agreement between initial clinical diagnoses and the research classification. A notable exception was a young man with a first-onset psychosis initially thought to be schizoaffective disorder, manic subtype. His affective symptoms rapidly remitted, but he continued to exhibit many features of acute schizophrenia for several months in the absence of mood disorder. His final research classification was, therefore, changed from schizoaffective disorder, manic subtype, to acute schizophrenia.

Blood sampling

The control subjects were not admitted to hospital. All patients and controls were asked to fast from midnight before blood sampling. During the following day, all were offered the same hospital diet at the same times of day. There was, however, considerable variation between subjects in the extent to which they complied with this request, and this variation was greatest among the patient group. Within one week of admission, blood samples (10 ml) were withdrawn from an indwelling cannula, kept patent with a heparin lock, and placed in a forearm vein about 20–30 minutes before the first sample at 07.00 h, with further samples taken at 07.30, 08.00 (a.m.), 15.00, 15.30, 16.00 (p.m.), and 23.00, 23.30 and 24.00 h (e.v.). Blood was collected in lithium heparin-coated tubes containing 100 kallikrein-inhibiting units of aprotinin (Trasylol), and kept at 4°C for up to 24 hours until centrifugation at 1600 *g* and 4°C. The plasma was stored at −40°C until assay.

Hormone assays

Plasma concentrations of PRL, GH, TSH, nicotine-stimulated neurophysin (NSN), and ESN were measured with National Institute of arthritis, diabetes and digestive kidney diseases (NIADDK) radioimmunoassay kits. The reference preparations (and intra-assay and interassay % coefficients of variation, and lower limits of sensitivity were: PRL, hPRL-RP-1 (AFP-2312C) (3.9%, 8.9%, 70 mU/l); GH, hGH-HS2243E (9.0%, 10.4%, 1.6 mU/l); TSH, the WHO first international reference preparation 63/38, obtained from the National Institute of Biological Standards and Control (6.2%, 9.7%, 0.8 mU/l). The reference preparations for ESN (5.2%, 7.8%, 80 pmol/l) and NSN were those given to NIADDK by Dr A. Robinson, University of Pittsburgh. The NSN results were all at or close to the lower limit of sensitivity of the assay (20 pmol/l) and, therefore, were not included in the statistical analysis. Total cortisol concentrations were determined as previously reported (Christie *et al*, 1986).

Medication

Seventy patients, by their own account, had been free of all oral psychotropic medication for at least three months (a year for depot medication); four patients with major depressive disorder (psychotic subtype) who had received benzodiazepine medication (up to 20 mg daily) before admission were also included. The drug history was always later confirmed by hospital and general practitioner records and, in most instances, at interview with a close relative. Urine from a random sample of 26 patients believed to be drug free, collected on the day after admission, was also examined using the Toxi-lab System for the presence of drugs. This system detected no drugs other than nicotine, caffeine, and salicylates (one subject each). On the day of blood sampling, when there was a danger to the patient or others, 30 of the 70 patients who had otherwise been drug free (14 schizophrenic, 7 with manic disorder, 6 with schizoaffective disorder, manic subtype, 1 with schizoaffective disorder, depressive subtype, 1 with unspecified psychosis, and 1 with manic disorder, post-partum onset) were given 200–600 mg amylobarbitone.

Statistical analysis

The data comprised five hormone values, each measured on nine occasions in 98 patients and 35 control subjects. The three values for each homone during the three collection periods (a.m., p.m., and e.v.) were averaged and transformed (see Table II) to normal distribution before analysis.

The SPSS-X statistical package was then used for analysis. Firstly, a multivariate repeated-measures analysis of covariance (MANOVA) by sex and diagnostic group (between-subject factors), time (a.m., p.m., and e.v. as a within-subject factor), and age as the covariate, was performed on the hormonal data. Certain symmetry conditions for the distribution of the variance and covariance matrices are required for the repeated-measures design (Scheffe, 1959; Huynh & Mandeville, 1979). The Box modified likelihood ratio criterion *M* (Box's *M*) was used to test whether these conditions were met. The analysis generated (a) multivariate significance tests of the effects of sex on the hormonal differences between diagnostic groups adjusted for age; (b) multivariate tests of the effects of diagnosis on hormonal measures over time adjusted for age and sex; (c) univariate statistics that have more statistical power than the one-way analysis of variance (ANOVA) described below.

The transformed data were entered into a one-way ANOVA, and the source of differences between diagnostic groups on each hormonal measure located by the multiple-range test of Duncan (Winer, 1971). Only those hormones determined by MANOVA to differ by diagnosis are reported during this stage of the analysis. The reliability of this choice was improved by lowering the nominal significance level ($P<0.05$) to $P<0.003$, to allow for the number of tests performed (Jacobs, 1971). Correlations between plasma cortisol and TSH concentrations were made by Pearson's method using transformed data.

Results

General health

Clinical examination and history showed no evidence of physical illness in any patient. All patients and control subjects were normotensive (systolic blood pressure less than 160 mmHg, diastolic less than 95 mmHg). Three patients were obese (two schizophrenic, one with schizoaffective disorder, depressive subtype), and four patients were underweight (one schizophrenic, two with major depressive disorder, psychotic subtype, one with manic disorder) as judged by standard tables for their height, body build, and age. There were no significant differences between patient groups in plasma sodium concentration or plasma T_4 (Table I). Plasma TSH concentrations were in the range 2.5–6 mU/l except in three patients, in each of whom one of nine plasma values was above 6 mU/l but below 9.8 mU/l. Further clinical assessment (Caldwell *et al*, 1985) of these patients showed no evidence or history of thyroid disease, and they were retained in the study.

Effects of amylobarbitone

Only psychotic patients were examined for the effects of amylobarbitone. One group ($n=28$) was drug free for at least three months before blood sampling, and the other ($n=36$) was treated by amylobarbitone on or immediately before the day of sampling, but was otherwise drug free. MANOVA detected no significant effects of amylobarbitone (Hotelling's $T^2=0.81$, $P<0.67$).

Diagnostic groups

Table II presents plasma hormone concentrations in each of the major drug-free diagnostic groups (57 patients). Significance tests were performed on transformed data (log: growth hormone, cortisol a.m., OSN, TSH; square root: prolactin e.v. and cortisol, p.m., e.v.; and reciprocal:

TABLE I

Characteristics of 57[1] drug-free psychotic patients, subdivided according to RDC

	n	*Weight (kg): range, mean ± s.d.*	*Na (mmol/l): range, mean ± s.d.*	*T_4 (mU/litre): range, mean ± s.d.*	*First episode: relapse*
Schizophrenia	26	47.0–96.8 66.0 ± 10.5	139–144 140 ± 1.9	60–121 94.4 ± 18.3	16:10
Schizoaffective disorder	9	43.5–65.7 56.0 ± 7.9	135–142 139.8 ± 2.3	61–136 97.8 ± 25.3	3:6
Major depressive disorder	10	44.6 ± 72.5 57.5 ± 10.0	133–142 139.7 ± 2.7	78–106 96.7 ± 0.8	3:7
Manic disorder	12	50.0–92.9 62.7 ± 13.9	137–143 141.3 ± 2.5	81–118 91.5 ± 14.9	4:8

[1] Forty-one patients are omitted – these patients were either not drug free or were from smaller diagnostic groups.

TABLE II

Median, first and third quartiles of plasma hormone concentrations, age and sex distributions by diagnostic group in 57 drug-free psychotic patients and 35 control subjects

Group	n	*Mean age (s.d.)*	*Sex M:F*	*Prolactin: mU/l*			*Growth hormone: mU/l*			*Cortisol: nM*			*Thyroid stimulating hormone: pmol/l*			*Oestrogen-stimulated neurophysin: pmol/l*		
				a.m.	*p.m.*	*e.v.*	*a.m.*	*p.m.*	*e.v.*	*a.m.*	*p.m.*	*e.v.*	*a.m.*	*p.m.*	*e.v.*	*a.m.*	*p.m.*	*e.v.*
Schizophrenia	26	30	21:5	543*	322	357	4.6	5.4	5.0	498***	285***	200***	4.0	3.8	4.3**	133	125	129
		(12)		382	250	284	2.8	3.5	2.8	288	215	98	3.5	3.1	3.8	108	91	91
				692	419	464	6.7	8.8	9.0	616	336	353	4.7	4.1	5.1	191	154	170
Major depressive disorder, psychotic subtype	10	45	3:7	460*	385*	443	12	7.8	4.6	499***	285***	240***	3.2	3.1	3.6***	170	179	166
		(11)		309	284	347	3.2	4.8	2.8	295	184	156	2.9	2.8	3.1	108	102	127
				1083	846	655	14	9.2	6.5	519	373	308	4.0	3.9	4.2	297	324	218
Schizoaffective disorder, manic subtype	9	38	5:4	525*	308	326	3.5	5.6	4.8	646*	454*	413*	3.3	2.9	3.1*	266	224	208
		(12)		366	217	277	2.9	2.6	3.4	622	368	305	3.0	2.6	2.6	112	112	120
				1089	371	347	7.3	7.5	8.4	686	520	486	4.4	3.1	3.2	436	423	444
Manic disorder	12	38	8:4	506*	340*	441	4.6	5.0	5.4	543***	262***	239***	4.2	3.6	4.0**	137	121	108
		(18)		343	305	368	2.4	4.5	3.0	466	213	121	3.6	3.8	3.7	96	91	85
				742	716	716	8.3	9.5	15	584	347	349	5.8	4.4	5.5	172	162	139
Controls	35	41	15:20	305	249	287	3.7	4.3	3.8	404	205	132	3.9	3.4	4.2	125	125	141
		(13)		228	217	238	2.9	3.0	3.4	321	179	82	3.4	3.1	3.7	100	91	100
				420	298	445	6.0	5.3	7.8	495	271	166	4.4	4.0	5.1	232	191	199
		F^1		7.0	5.9	3.6	1.6	0.8	0.4	6.5	9.4	7.9	2.4	4.0	7.4	2.0	2.2	2.1
		p(d.f.4,87)^2		<0.002	<0.001	<0.02	<0.12	<0.36	<0.77	<0.001	<0.001	<0.001	<0.04	<0.005	<0.001	<0.009	<0.007	<0.02
		Transformation		$1/x$	$1/x$	$\sqrt{x}$	$\ln x$	$\ln x$	$\ln x$	$\ln x$	$\sqrt{x}$	$\sqrt{x}$	$\ln x$	$\ln x$	$\ln x$	$\ln x$	$\ln x$	$\ln x$

1. F values are from a one-way analysis of variance for each hormone.
2. The corrected significance level is $P<0.003$.

$^*P<0.01$ patient group v. controls; $^{**}P<0.01$ v. SAM; $^{***}P<0.05$, patient group v. controls.

Transformation to normal distribution are reciprocals ($1/x$), logE ($\ln x$) or root ($\sqrt{x}$). All statistics were performed on transformed data.

prolactin a.m. and p.m.). The covariance matrices generated for each of the diagnostic groups did not differ significantly from each other (Box's $M=214$, $P<0.36$), and so met requirements for the multivariate analysis.

The MANOVA showed that the hormonal differences between diagnostic groups remained when the effects of sex, age, and time were adjusted for. Prolactin and growth hormone were affected by sex. There was a significant covariance between plasma growth hormone concentration and age ($P<0.001$). There was no significant interaction between sex, diagnosis, and time adjusted for age for any hormone.

The ANOVA detected significant ($P<0.003$) between-groups F ratios for prolactin a.m., p.m., cortisol a.m., p.m., e.v., and TSH e.v. Duncan's multiple-range test located the source of these differences between groups ($P<0.01$) as follows: for prolactin (a.m. and p.m.) major depressive disorder, psychotic subtype, and manic disorder; for cortisol a.m., manic disorder and schizoaffective disorder, manic subtype (SAM); for cortisol p.m., e.v., SAM; for TSH e.v., SAM. Scheffe's procedure detected significant ($P<0.01$) differences for TSH e.v. between SAM and schizophrenia, and between SAM and manic disorder (Table II). There were no significant correlations between plasma cortisol and TSH concentrations within the total study population or in any single diagnostic subgroup.

In summary, the largest single source of differences between diagnostic groups was attributable to the SAM patients. These were characterised by increased cortisol and decreased TSH e.v. concentrations when compared with control subjects. The SAM patients also had significantly lower plasma TSH e.v. concentrations than those with either schizophrenia or manic disorder. These differences could not be attributed to the effects of amylobarbitone, age, or sex.

Effects of time

Over time (a.m., p.m., and e.v.) there were significant differences between diagnostic groups (Hotelling's $T^2=0.84$, $P<0.001$). These were located to prolactin, $F=2.8$, $P<0.03$; cortisol, $F=7.8$; $P<0.001$; and TSH, $F=6.0$, $P<0.001$. Our sampling points were too few to fit cosine functions to the data of a circadian rhythm in hormone secretion (Monk & Fort, 1983). Inspection of individual profiles of plasma cortisol showed that during the night-time (23.00–24.00 h) sampling period, 1 of 35 controls and 21 of 57 psychotic patients had an average cortisol concentration more than two standard deviations above the control mean. These 21 patients comprised four with major depressive disorder (psychotic subtype), eight with schizophrenia, six with schizoaffective mania, and three with manic disorder.

Discussion

These results show that the endocrine disturbances of the psychoses do vary according to the nature of the illness. When allowance was made for the age and sex differences between diagnoses, SAM could be distinguished, using endocrine data alone, from other psychoses.

We could not establish that other factors, not involved in the diagnostic classification of patients but known to influence plasma hormones, had contributed to these endocrine differences. The general health (Amico *et al*, 1984; Semple, 1986) of each group appeared similar, and no differences were found after adjustments were made for the effects of age and sex. The fact that blood sampling and diagnostic procedures were carefully standardised substantially reduced these sources of bias. Differences between control subjects and psychotic patients may, however, have been attributable to the stress of hospital admission or altered motor activity associated with illness. Because blood samples were obtained one to seven days after admission to hospital and the RDC required an illness duration of at least two weeks, our patients cannot be considered to be acutely stressed in a way comparable to experimental studies of the endocrine effects of stress (e.g. Hodges *et al*, 1962; Rubin *et al*, 1970; Miyabo *et al*, 1976; Johansson *et al*, 1983; Brooks *et al*, 1986). Our previous analysis of the cortisol data (Christie *et al*, 1986) showed that increased cortisol secretion was unrelated to the time of blood sampling in relation to hospital admission and to correlates of stress, such as psychic or somatic anxiety and agitation. Increased cortisol secretion was, however, closely related to some of the features of psychosis.

Thus, the present and previous (Christie *et al*, 1986) data show that increased plasma cortisol and prolactin concentrations in psychotic subjects are not simply the effects of stress. Our data that show that increased cortisol secretion is a feature of psychosis but is not specific for major depression are consistent with those of several recent studies (Pfohl *et al*, 1985; Halbreich *et al*, 1985*a*,*b*; Rubin *et al*, 1987).

Plasma TSH concentrations also showed evidence of specificity. Significant decreases were found in SAM during the night-time sampling period (e.v.), a time when in controls, schizophrenic and manic patients, plasma TSH showed a consistent night-time rise. Comparable decreases in plasma TSH have been reported previously (Golstein *et al*, 1980; Kjellman *et al*, 1984; Unden *et al*, 1987) in patients with major depressive disorder, but there are no similar studies in schizoaffective mania. In a review of the TSH response to TRH in depressed patients, Loosen & Prange (1982) noted the suggestion that TSH secretion may be suppressed by increased circulating plasma cortisol (Otsuki *et al*, 1973; Nicoloff *et al*, 1979). A possible explanation of lower plasma TSH in SAM could, therefore, be based upon such a putative suppressive effect of cortisol on TSH release.

We regard this explanation as unlikely, since we could detect no significant intercorrelations between plasma cortisol in TSH in any of our diagnostic subgroups or in the total population. Winokur *et al* (1983) reached a similar conclusion when considering the interactions between plasma anterior pituitary hormone concentrations and responses to TRH in depressed patients. On the basis of these results, we concluded that disturbances in cortisol and TSH detected in SAM are specific for SAM and do not simply reflect an increase in plasma cortisol that, in turn, suppresses TSH secretion.

We did not find changes in either growth hormone or the neurophysins. In an intensive study of growth hormone secretion in major depressive disorder, Mendlewicz *et al* (1985) detected hypersecretion of growth hormone. Table II shows that there were no significant differences between diagnostic groups in the present study, although the highest median values were found in the morning samples from depressed patients. After adjusting for the effects of age and sex, there were no significant differences. Failure to detect a significant difference when it is, in fact, present between study populations can arise because, as in our case, the study sample is small. We are not able to exclude this potential source of error.

Our knowledge of the neurotransmitter control of pituitary hormone secretion is not sufficiently advanced to allow firm interpretation of our data in terms of central neurotransmitter dysfunction. However, these data do identify questions which could be answered by further basic and clinical research. For example, the increased prolactin concentrations, which our data suggest are a general feature of psychosis, together with the findings that prolactin concentrations are unchanged or increased in schizophrenia (Meltzer *et al*, 1974; Johnstone *et al*, 1977; Gruen *et al*, 1978), acute paranoid psychoses (Ohman & Axelsson, 1978), major depressive disorders (Mendelwicz *et al*, 1980; Unden *et al*, 1987), and manic disorder (Cookson, 1985), suggest that the generally accepted version of the dopamine hypothesis of schizophrenia needs to be re-evaluated. Similarly, the older view, based on early animal experiments, that increased plasma cortisol secretion reflects decreased central noradrenergic and/or serotonergic activity, must be carefully re-evaluated in view of the fact that recent studies show that noradrenaline stimulates cortisol secretion (Tuomisto & Mannisto, 1985), and that cortisol and prolactin secretion is stimulated by central serotonergic activation (Rivier & Plotsky, 1986; Goodwin *et al*, 1987).

Further biological studies in heterogeneous samples of psychotic subjects are likely to clarify the issues raised here. We have found that a single functional psychiatric disorder, SAM, can be separated from neighbouring syndromes by biological data and this finding requires replication. As our understanding of the neuroendocrine control of hormone secretion progresses, it may be possible to identify precisely the neurobiological abnormalities that underlie the differences we have detected.

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References

ALLEN, P., BATTY, K., DODD, C., *et al* (1985) Dissociation between emotional and endocrine responses preceding an academic examination in medical students. *Journal of Endocrinology*, **114**, 166–176.

AMICO, J., CORDER, C., MCDONALD, R., *et al* (1984) Levels of the oxytocin associated and vasopressin associated neurophysins in plasma and their responses in essential hypertension. *Clinical Endocrinology*, **20**, 289–297.

BROOKS, J., HERBERT, M., WALDER, C. P., *et al* (1986) Prolactin and stress: some endocrine correlates of pre-operative anxiety. *Clinical Endocrinology*, **24**, 653–656.

CALDWELL, G., GOW, S. M., SWEETING, V. M., *et al* (1985) A new strategy for thyroid function testing. *Lancet*, *I*, 1117–1119.

CHARNEY, D. S., MENKES, D. B. & HENNINGER, G. R. (1981) Receptor sensitivity and the mechanism of action of antidepressant treatment. *Archives of General Psychiatry*, **38**, 1160–1180.

CHRISTIE, J., WHALLEY, L., DICK, H., *et al* (1986) Raised plasma cortisol concentrations are a feature of drug-free psychotics and are not specific for depression. *British Journal of Psychiatry*, **148**, 58–65.

——, ——, BENNIE, J., *et al* (1987) Characteristic plasma hormone changes in Alzheimer's disease. *British Journal of Psychiatry*, **150**, 674–681.

COOKSON, J. (1985) The neuroendocrinology of mania. *Journal of Affective Disorders*, **8**, 233–241.

GOLSTEIN, J., VAN CAUTER, E., LINKOWSKI, P., *et al* (1980) Thyrotrophin nyctohemeral pattern in primary depression: differences between unipolar and bipolar women. *Life Sciences*, **27**, 1695–1703.

GOODWIN, G. M., FAIRBURN, C. G. & COWEN, P. J. (1987) The effects of dieting and weight loss upon neuroendocrine responses to tryptophan, clonidine and apomorphine in volunteers: important implications for neuroendocrine investigations in depression. *Archives of General Psychiatry*, **44**, 952–957.

GRUEN, P., SACHAR, E., ALTMAN, N., *et al* (1978) Relation of plasma prolactin to clinical response in schizophrenic patients. *Archives of General Psychiatry*, **35**, 1222–1227.

HALBREICH, U., ASNIS, G. M., SHINDLEDECKER, R., *et al* (1985*a*) Cortisol secretion in endogenous depression. I. Basal plasma levels. *Archives of General Psychiatry*, **42**, 904–908.

——, ——, ——, *et al* (1985*b*) Cortisol secretion in endogenous depression. II. Time-related functions. *Archives of General Psychiatry*, **42**, 909–914.

Hodges, J., Jones, M. & Stockham, M. (1962) Effect of emotion on blood corticotrophin and cortisol concentrations in man. *Nature*, **193**, 1187–1188.

Huynh, H. & Mandeville, G. K. (1979) Validity conditions for repeated measures designs. *Psychological Bulletin*, **86**, 964–973.

Jacobs, K. W. (1971) A table for the determination of experimentwise error rate (alpha) from independent comparisons. *Educational Psychological Measurements*, **36**, 899–903.

Johannsson, G. G., Karonen, S-L. & Laakso, M-L. (1983) Reversal of an elevated plasma level of prolactin during prolonged psychological stress. *Acta Psychiatrica Scandinavica*, **69**, 491–502.

Johnstone, E., Crow, T. & Mashiter, K. (1977) Anterior pituitary hormone secretion in chronic schizophrenia: an approach to neurohumoral mechanisms. *Psychological Medicine*, **7**, 223–228.

Kendell, R. E. (1982) The choice of diagnostic criteria for biological research. *British Journal of Psychiatry*, **39**, 1334–1339.

Kendler, K. S. (1987) The impact of diagnostic misclassification on the pattern of familial aggregation and co-aggregation of psychiatric illness. *Journal of Psychiatry Research*, **21**, 55–91.

Kjellman, B., Beck-Friis, J., Ljunggren, J-G., *et al* (1984) Twenty-four-hour serum levels of TSH in affective disorders. *Acta Psychiatrica Scandinavica*, **69**, 491–502.

Loosen, P. T. & Prange, A. J. (1982) Serum thryrotropin response to thyrotropin-releasing hormone in psychiatric patients: a review. *American Journal of Psychiatry*, **139**, 405–416.

Mason, J. W., Mougey, E. H., Brady, J. V., *et al* (1968) Thyroid (plasma butanol-extractable iodine) responses to 72 hour avoidance sessions in the monkey. *Psychosomatic Medicine*, **30**, 682–695.

——, Hartley, L. H., Kotchen, T. A., *et al* (1973) Plasma thyroid stimulating hormone response in anticipation of muscular exercise in the human. *Journal of Clinical Endocrinology and Metabolism*, **37**, 403–406.

Meltzer, H. Y., Sachar, E. J. & Frantz, A. G. (1974) Serum prolactin levels in unmedicated schizophrenic patients. *Archives of General Psychiatry*, **31**, 564–569.

Mendelwicz, J., van Cauter, E., Linkowski, P., *et al* (1980) The 24-hour profile of prolactin in depression. *Life Sciences*, **302**, 1091–1092.

——, Linkowski, P., Kerkhofs, M., *et al* (1985) Diurnal hypersecretion of growth hormone in depression. *Journal of Clinical Endocrinology and Metabolism*, **60**, 505–512.

Miyabo, S., Hisada, T., Asato, T., *et al* (1976) Growth hormone and cortisol responses to psychological stress: comparison of normal and neurotic subjects. *Journal of Clinical Endocrinology and Metabolism*, **42**, 1158–1162.

Monk, T. H. & Fort, A. (1983) 'Cosina': a cosine curve fitting programme suitable for small computers. *International Journal of Chronobiology*, **8**, 193–205.

Nicoloff, J., Fisher, D. & Appleman, M. (1979) The role of glucocorticoids in the regulation of thyroid function in man. *Journal of Clinical Investigation*, **49**, 1922–1929.

Ohman, R. & Axelsson, R. (1978) Relationship between prolactin response and anti-psychotic effect of thioridazine in psychiatric patients. *European Journal of Clinical Pharmacology*, **14**, 111–116.

Otsuki, M., Dakoda, M. & Baba, S. (1973) Influence of glucocorticoids on TRH induced TSH response in man. *Journal of Clinical Endocrinology Metabolism*, **36**, 95–102.

Pfhol, B., Sherman, B., Schlechte, J., *et al* (1985) Pituitary-adrenal axis rhythm disturbances in psychiatric depression. *Archives of General Psychiatry*, **42**, 897–903.

Rivier, C. L. & Plotsky, P. M. (1986) Mediation by corticotrophin releasing factor (CRF) of adenohypophysial hormone secretion. *Annual Reviews in Physiology*, **48**, 475–494.

Rubin, R. T., Miller, L. G., Clark, B. R., *et al* (1970) The stress of aircraft carrier landing I. Corticosteroid responses in naval aviators. *Psychosomatic Medicine*, **32**, 581–588.

——, Poland, R. E., Lesser. I. M., *et al* (1987) Neuroendocrine aspects of primary endogenous depression. I. Cortisol secretory dynamics in patients and matched controls. *Archives of General Psychiatry*, **44**, 328–336.

Scheffe, H. (1959) *The Analysis of Variance*. New York: Wiley.

Schleifer, S. J., Keller, S. E., Siris, S. G., *et al* (1985) Depression and immunity. *Archives of General Psychiatry*, **42**, 129–133.

Semple, G. G. (1986) Hormonal changes in non-endocrine disease. *British Medical Journal*, **293**, 1049–1052.

Shagass, C., Roemer, R. A., Straumanis, J. J., *et al* (1985) Combinations of evoked potential amplitude measurements in relation to psychiatric diagnosis. *Biological Psychiatry*, **20**, 701–722.

Snyder, S. H., Banerjee, S. P., Yamamura, H. I., *et al* (1974) Drugs, neurotransmitters and schizophrenia. Phenothiazines, amphetamines and enzymes synthesizing psychotomimetic drugs aid schizophrenia research. *Science*, **184**, 1243–1253.

Spitzer, R., Endicott, J. & Robins, E. (1978) Research Diagnostic Criteria: rationale and reliability. *Archives of General Psychiatry*, **35**, 773–782.

Taylor, M. A., Abrams, R. & Gaztanga, C. (1974) Manic-depressive illness and acute schizophrenia, a clinical, family history and treatment response study. *American Journal of Psychiatry*, **131**, 678–682.

Tsuang, M., Winokur, G. & Crowe, G. (1980) Morbidity risks of schizophrenia and affective disorders among first-degree relatives of patients with schizophrenia, mania, depression and surgical conditions. *British Journal of Psychiatry*, **137**, 497–504.

Tuomisto, J. & Mannisto, P. (1985) Neurotransmitter regulation of anterior pituitary hormones. *Pharmacological Reviews*, **37**, 249–332.

Unden, F., Ljunggren, J., Kjellman, B., *et al* (1987) Unaltered 24h serum PRL levels and PRL response to TRH in contrast to decreased 24h serum TSH levels and TSH response to TRH in major depressive disorder. *Acta Psychiatrica Scandinavica*, **75**, 131–138.

Whalley, L., Christie, J., Bennie, J., *et al* (1985) Selective increase in plasma luteinizing hormone in drug-free young men with mania. *British Medical Journal*, **290**, 99–102.

——, ——, ——, *et al* (1987*a*) Case report. Elevated plasma luteinizing hormone concentrations, cryptorchidism and mania. *Psychoneuroendocrinology*, **12**, 73–77.

——, Kutcher, S., Blackwood, D. H. R., *et al* (1987*b*) Increased plasma LH in manic-depressive illness: evidence of a state-independent abnormality. *British Journal of Psychiatry*, **150**, 682–684.

——, Christie, J. E., Blackwood, D. H. R., *et al* (1989) Disturbed endocrine function in the psychoses: II. Discriminant function analysis of multihormone data. *British Journal of Psychiatry*, **155**, 462–467.

Winer, B. J. (1971) *Statistical Principles in Experimental Design*, p. 184. New York: McGraw Hill.

Wing, J., Cooper, J. & Sartorius, N. (1974) *The Description and Classification of Psychiatric Symptoms: An Instruction Manual for PSE and CATEGO System*. London: Cambridge University Press.

Winokur, A., Amsterdam, J. D., Oler, J., *et al* (1983) Multiple hormonal responses to Protirelin (TRH) in depressed patients. *Archives of General Psychiatry*, **40**, 525–531.

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Disturbed Endocrine Function in the Psychoses

II: Discriminant Function Analysis of Multihormone Data

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Discriminant function analyses were performed on plasma concentrations of prolactin, growth hormone, cortisol, TSH, and the neurophysins measured over 17 hours in 70 newly admitted drug-free psychiatric patients and 35 control subjects. The hormone data distinguished between patients with different classes of drug-free psychosis (26 schizophrenic, 12 with manic disorder, 10 with major depressive disorder, psychotic subtype, 9 with schizoaffective mania (SAM)). Higher plasma cortisol and lower TSH concentrations separated eight of nine SAM patients from all others.

Theoretical relationships between the psychoses may be clarified by examination of the hormonal differences between psychoses. For example, one view of the psychoses is that they lie along a single continuum encompassing health, mania, depressive psychoses, schizoaffective psychoses, and schizophrenia. If biologically determined variables could satisfactorily distinguish between psychoses, and between psychoses and health, then the same variables may help determine the relative positions of each psychosis along a single continuum, and may identify boundaries between disorders (Kendell, 1975).

Few other studies have examined the utility of biological data in the classification of the major functional psychoses. From the limited information available, it is clear that schizophrenia can be distinguished from other, non-psychotic disorders and health using, for example, measures derived from the evoked potential (Shagass *et al*, 1985), but not from the affective psychoses. Similar studies have been reported using computerised axial tomography (Reider *et al*, 1983; Tsai *et al*, 1983), platelet serotonin concentrations (Stahl *et al*, 1983), positron emission tomography (Buchsbaum *et al*, 1984; Kling *et al*, 1986), and smooth-pursuit eye movement (Siever *et al*, 1984). These studies show that the biological basis of an inferred neural abnormality may not be specific for a single disorder, but can be found in most psychoses. Since many reported abnormalities are relatively enduring, they may be related to the biological susceptibility to psychoses, and may facilitate the separation of homogeneous groups for more detailed investigations (e.g. molecular genetic studies as suggested by Radouco-Thomas *et al*, 1984).

In the companion paper (Whalley *et al*, 1989 – this issue, pp. 455–461), we presented data pointing to differences in plasma hormone concentrations between diagnostic subgroups that could not be explained simply as endocrine responses to stress. We now report a discriminant function analysis of the same data. This approach avoids problems of statistical inference, but ideally requires replication with a new data set. Drug-free patients are difficult to locate and, especially when disturbed, difficult to study. We adopted the following solution. In the first stage of discriminant analysis, we included only control subjects and those drug-free psychotic patients in diagnostic groups large enough to be informative. In the second stage, we used the first two discriminant functions derived from the drug-free psychotic patients to classify the remainder of our sample. This comprised those patients who had received medication up to two weeks before blood sampling and who did not meet drug-free criteria, and those drug-free patients in diagnostic groups too small to be included in the discriminant analysis. The reasoning that lead to our use of discriminant analysis in this way is detailed by Kendell (1975, pp. 106–118).

Method

Ninety-eight patients routinely admitted to hospital and 35 control subjects were studied. They are fully described in the companion paper (Whalley *et al*, 1989), along with details of the diagnostic and investigative procedures.

Statistical analysis

The 35 control subjects and 57 drug-free psychotic patients in the four largest diagnostic groups (schizophrenia, $n = 26$; manic disorder, $n = 12$; major depressive disorder, psychotic subtype, $n = 10$; schizoaffective disorder, manic subtype, $n = 9$) were entered into a discriminant analysis: 41 patients were omitted, either because they had or may have received medication during the previous three months, or because they were in diagnostic groups too small for analysis. The latter group comprised: schizophrenia (6 patients), major depressive disorder, psychotic subtype (5), major depressive disorder, endogenous subtype (12), schizoaffective disorder, depressive subtype (3), minor depressive disorder (3), manic disorder (7, of whom 3 had a post-partum onset), and five patients with unclassified psychoses.

The prior probabilities of group membership were adjusted according to the distribution of cases among the largest diagnostic groups and control subjects. Variables were selected for inclusion in the discriminant analysis on the basis of the results of the ANOVA. Only those hormones with a between-group F ratio greater than 4.2 (d.f. 4, 87; $P<0.003$) were used.

Discriminant analysis derives a linear composite, the discriminant function, which maximally discriminates between groups. A discriminant score is provided for each subject that maximises the F ratio of the between-group and within-group mean squares in a univariate ANOVA.

Discriminant functions were derived by stepwise procedures using Wilk's method (Cooley & Lohnes, 1971). The stepwise selection criteria were determined by the overall multivariate F ratio for the test of differences between the centroids of each group. Scores on discriminant functions 1 and 2 were calculated for the remaining 41 patients not included in the analysis so far, and the resulting classification compared with their clinical grouping. The discrimination achieved between diagnostic groups by discriminant analysis was then compared with the results of two further discriminant analyses. In the second, 12 schizophrenic subjects were randomly removed and the analysis repeated. In the third, the control group was removed. These further analyses provided a test of 'spuriousness' of the results of the first analysis.

Results

Discriminant analyses

The first discriminant analysis (A) derived two functions that together accounted for 100% of the variance (functions 1A and 1B, Table I). Cortisol (p.m.) entered the analysis at $F=9.4$, TSH (ev.) at $F=8.8$, prolactin (p.m.) at $F=7.7$, and prolactin (a.m.) at $F=6.6$, and their standardised canonical discriminant function coefficients are given in Table I. Figure 1 shows plots of scores on functions 1A and 2A for the five diagnostic groups. Scores were then obtained for the 41 ungrouped subjects. Table II presents a classification of the 57 psychotic patients and 35 control subjects entered at this stage of the analysis and shows that eight of nine SAM patients were correctly identified, with no false positives. All 12 manic patients were correctly identified, with 35 (44%) false positives. When discriminant scores were obtained for the ungrouped cases, four (10%) were classified as SAM. These four comprised one schizophrenic, one major depressive disorder, psychotic subtype, and two unclassified psychoses.

The second (B) and third (C) discriminant analyses were undertaken to test the reliability of the first (A). After

TABLE I

Standardised discriminant function coefficients of transformed[1] *plasma hormone concentration derived in three analyses (A, B, and C)*

Hormone	*Time*	*Functions*[2] *1A*	*2A*	*1B*	*2B*	*1C*	*2C*
Prolactin							
	a.m.	0.31	0.06	—	—	—	
	p.m.	0.00	0.95	0.30	0.68	—	—
	ev.	—	—	—	—	—	—
Cortisol							
	a.m.	—	—	—	—	0.67	0.74
	p.m.	−0.74	−0.16	—	—	—	—
	ev.	—	—	−0.78	−0.25	—	—
TSH							
	a.m.	—	—	—	—	—	—
	p.m.	—	—	—	—	—	—
	ev.	0.71	−0.18	0.69	−0.44	−0.87	0.18
Oestrogen-stimulated neurophysin							
	a.m.	—	—	—	—	—	—
	p.m.	—	—	—	—	0.59	−0.48
	ev.	—	—	−0.11	−0.68	—	—
% variance		73%	18%	68%	25%	96%	4%
Significance		$P<0.0001$	$P<0.004$	$P<0.0001$	$P<0.0001$	$P<0.0001$	$P<0.62$

1. See Table II of paper I (p. 458).
2. Functions 1A and 2A are obtained for 92 subjects (35 controls, 26 schizophrenics, 12 with manic disorder, 10 with major depressive disorder, psychotic subtype, 9 with SAM); functions 1B and 2B derived for the same subjects after randomly removing 12 schizophrenics; and 1C and 2C after removing control subjects.

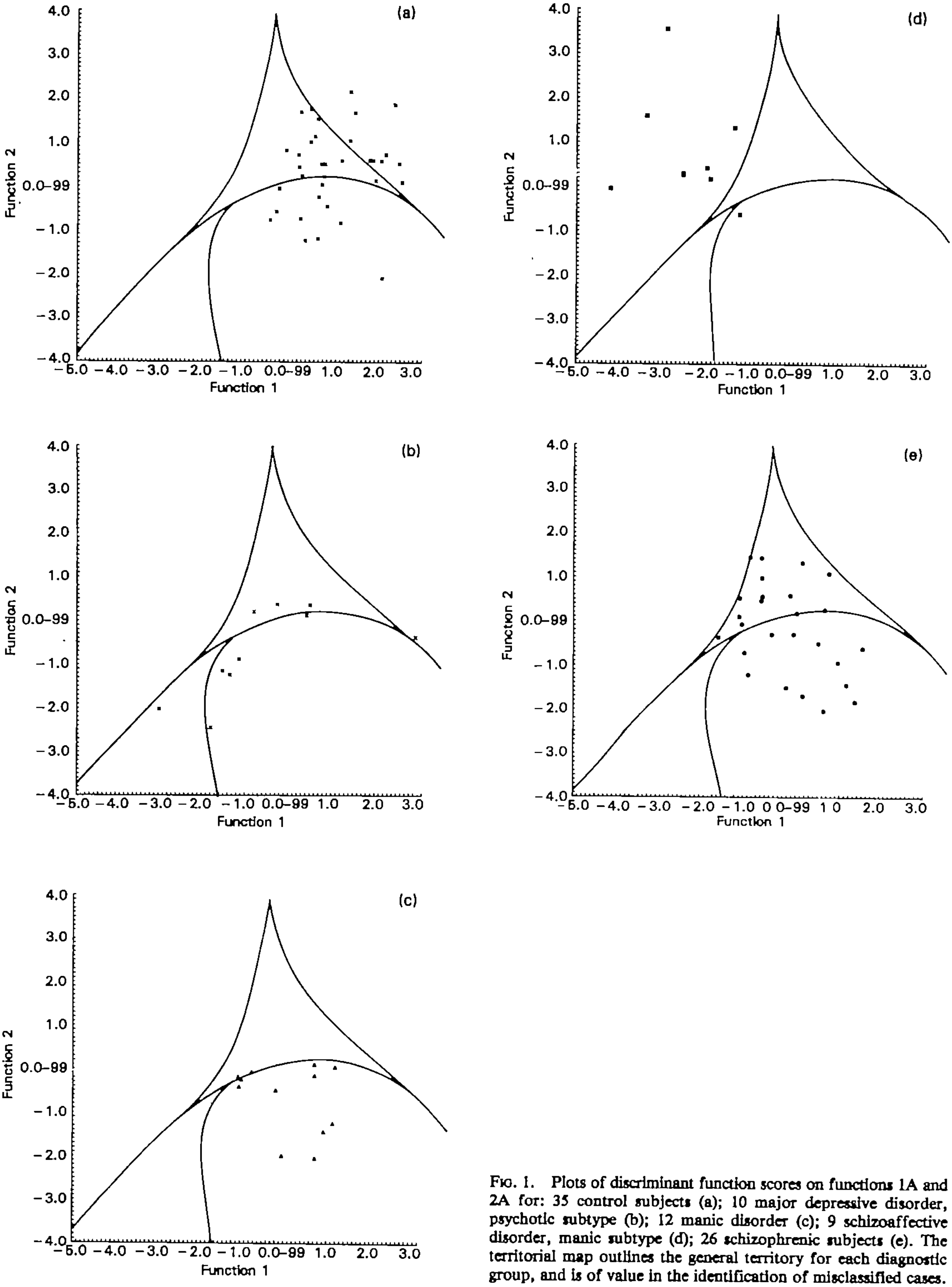

FIG. 1. Plots of discriminant function scores on functions 1A and 2A for: 35 control subjects (a); 10 major depressive disorder, psychotic subtype (b); 12 manic disorder (c); 9 schizoaffective disorder, manic subtype (d); 26 schizophrenic subjects (e). The territorial map outlines the general territory for each diagnostic group, and is of value in the identification of misclassified cases.

TABLE II
Classification based on scores derived from functions 1A and 2A of the discriminant analysis

		Predicted diagnostic group: no. (% correctly classified)				
Actual group	n	*Control*	*Schizophrenia*	*Major depressive disorder, psychotic subtype*	*Schizoaffective disorder, manic subtype*	*Manic disorder*
Control	35	14 (40%)	8 (23%)	0 (0%)	0 (0%)	13 (37%)
Schizophrenia	26	1 (4%)	9 (35%)	0 (0%)	0 (0%)	16 (62%)
Major depressive disorder, psychotic subtype	10	1 (10%)	3 (30%)	1 (10%)	0 (0%)	5 (50%)
Schizoaffective disorder, manic subtype	9	0 (0%)	0 (0%)	0 (0%)	8 (89%)	1 (11%)
Manic disorder	12	0 (0%)	0 (0%)	0 (0%)	0 (0%)	12 (100%)
'Ungrouped' cases[1]						
Schizophrenia	7	0	2	0	1	4
Major depressive disorder, psychotic subtype	5	0	2	1	1	1
Major depressive disorder, endogenous subtype	9	0	1	0	0	8
Schizoaffective disorder, depressed subtype	3	0	1	0	0	2
Manic disorder	3	1	0	0	0	2
Manic disorder, puerperal onset	3	0	0	3	0	0
Unclassified psychoses	5	0	0	0	2	3

1. The ungrouped cases were not entered into the analysis.

randomly removing 12 schizophrenics, two functions were derived, accounting for 93% of the variance. Six of nine SAM patients were correctly classified, with one false positive (a control subject). The three misclassified SAM patients were grouped with major depressive disorder, psychotic subtype. The third (C) discriminant analysis did not include control subjects, and the two functions derived accounted for 100% of the variance. Six of nine of SAM patients were correctly classified by scores on these functions; all three misclassified patients were placed under manic disorder. There were no false positive SAM 'diagnoses'.

In summary, the discriminant analyses yielded functions based largely on the power of cortisol and TSH (ev.) concentrations to distinguish between SAM and other disorders, especially the affective psychoses. Classifications based upon these analyses yielded broadly similar results, remarkable by the consistency of the separation between SAM and other disorders, and the fact that so few other patients were misclassified by discriminant function scores as SAM.

Discussion

Discriminant scores based on higher plasma cortisol and lower TSH concentrations separated eight of nine SAM patients from all others and so provided further endocrine support for the distinction between SAM and other psychoses made by RDC (see Whalley *et al*, 1989).

Discriminant function analysis is a statistical method for testing a classificatory system with particular advantages over factor and cluster analyses (Moran, 1966; Kendell & Gourlay, 1970; Kendell, 1975). The validity of any distinction obtained between groups by discriminant analysis rests upon the analysis meeting four criteria. First, the covariance matrices for each of the diagnostic groups must be equal, otherwise spurious results may be derived (Kendell & Post, 1973). Second, the choice of items included in the analysis must be carefully evaluated and the number of subjects entered needs to be greater than the product of the number of items and the number of groups. These two criteria were met in the present study: there was symmetry of variance matrices, and the problem of item selection was solved by setting the F ratio for an item to enter the analysis at a conservatively high value. The third criterion for a valid distinction between diagnoses is that the two categories must have a bimodal distribution of scores on the discriminant function with a 'point of rarity' between categories. There was a clear visual demonstration of this between SAM and other disorders: 1% of subjects were misclassified after analysis A, 5% after analysis B and 10% after analysis C. The derivation of functions in successive analyses that differ by item content and loadings is not relevant to the argument. Item loadings change markedly after subtraction or addition of subjects, since the loadings depend substantially upon the complex patterns of intercorrelations between items. The fourth criterion concerns replication with a fresh data set. This was not possible in the present study, but the classification of the 41 'ungrouped' cases provides further support of the distinction between SAM and other psychoses. The fact that none of the non-psychotic patients (15 subjects) were included in SAM is consistent with the view that the discriminant functions identified a valid boundary between SAM and other psychoses.

The analysis reported here supported the nosological status of schizoaffective mania. While this clearly requires replication, it is not an isolated finding. There are very few laboratory studies comparing subgroups of psychoses, and even fewer that separate schizoaffective disorders from others. In some biological studies where schizoaffective patients have been reported separately (sometimes by polarity), differences between schizoaffective disorder and other psychoses have been found (Meltzer *et al*, 1984); increased [^{3}H]-imipramine platelet binding in schizoaffective disorders compared with that in schizophrenia, depression, and controls (Suranyi-Cadotte *et al*, 1983), increased growth hormone response to apomorphine in schizoaffective disorders compared with that in mania (Hirschowitz *et al*, 1986), and decreased middle-ear muscle activity during REM sleep in schizoaffective disorders compared with that in schizophrenia, depression, and health (Benson & Zarcone, 1982). Marked differences between schizoaffective disorder and other diagnostic groups must argue for the retention of schizoaffective disorders as a separate category in future studies, and against the assumption that schizoaffective disorders are simply an 'interform' between schizophrenia and the affective disorders.

One of the major problems in the classification of the psychoses concerns the frequency with which disorders are encountered with features of both schizophrenia and the affective psychoses. The term 'schizoaffective' was introduced by Kasanin (1933) to distinguish good-prognosis, affect-laden schizophrenia from other schizophrenics. The schizoaffective-mania category of the RDC is a recent solution of the diagnostic problem posed by atypical psychoses with many features of mania, but with Schneider's first-rank symptoms of schizophrenia, and/or mood-incongruent hallucinations and delusions. DSM-III (American Psychiatric Association, 1980) retains the category of schizoaffective disorder only for those instances where "the clinician is unable to make a differential diagnosis with any degree of certainty". There is considerable continuing uncertainty about the existence of the schizoaffective syndrome, and this may account for there being so few biological studies on this topic (Clayton, 1982). Some authors (e.g. Pope & Lipinski, 1978) argue that the schizoaffective disorders are a subgroup of the affective psychoses, and as no consensus exists concerning the precise definition of schizoaffective disorder (Brockington & Leff, 1979; Levinson & Levin, 1987) and, according to Taylor (1984), most studies show schizoaffective disorders to be variants of the affective psychoses, unlike schizophrenia in family history, treatment response, long-term outcome, or neuropsychological and EEG findings. The existence of a distinct third type of psychosis, characterised by Langfeldt (1939) as "schizophreniform" and by Leonhard (1957) as "cycloid psychosis", may partly explain some of the uncertainty in this area. Levinson & Levin (1987) have detailed the degree of overlap between schizoaffective mania as defined by the RDC and European solutions to these problems.

It was not possible, in the present study, to determine the effect of clinical diagnostic misclassification on the interpretation of the biological data. Most studies in biological psychiatry are evaluated on the assumption that psychiatric diagnoses are free of error, but Clayton (1982) has pointed out that this is unlikely to be the case, and that schizoaffective disorders may be particularly susceptible to misclassification. The category of schizoaffective mania may include, at times, excited schizophrenics, the more severely ill manic subjects, and atypical or unclassifiable variants of the major psychoses. Kendler (1987) has argued that the effects of diagnostic misclassification should be taken into account when evaluating the results of genetic studies, and tentatively advances a mathematical model that may detect and allow for these effects. The reliability of psychiatric diagnoses, especially for those disorders where there is little agreement on diagnostic criteria, is such that misclassification rates probably seriously confound interpretation of the results.

It cannot be concluded on the basis of the results presented here that there is a subgroup of psychoses characterised by the features of manic disorder, with coexistent symptoms typical of schizophrenia, that is distinguishable from either schizophrenia or the affective psychoses. Our results do confirm, however, that in keeping with several recently introduced classificatory systems (and perhaps in agreement with certain European diagnostic traditions), it would be premature to discard the diagnostic category of schizoaffective disorder, especially in biological studies. In fact, the inclusion of schizoaffective patients in samples of schizophrenic or affective disorder patients may confound the results of biological investigations. The neurobiological basis of the distinction between SAM and other psychoses is unknown, and is discussed in the previous paper (Whalley *et al*, 1989). In the absence of satisfactory understanding of the neural control of the hormones that are the source of this distinction, this intriguing finding must remain unexplained.

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References

American Psychiatric Association (1980) *Diagnostic and Statistical Manual of Mental Disorders* (DSM-III). Washington, DC: APA.

Benson, K. L. & Zarcone, V. P. (1982) Middle ear muscle activity during REM sleep in schizophrenic, schizoaffective and depressed patients. *American Journal of Psychiatry*, **139**, 1474–1476.

Brockington, I. & Leff, J. (1979) Schizoaffective psychosis: definitions and incidence. *Psychological Medicine*, **9**, 91–99.

Buchsbaum, M. B., de Lisi, L. E., Holcomb, H. H., *et al* (1984) Anteroposterior gradients in cerebral glucose use in schizophrenia and affective disorders. *Archives of General Psychiatry*, **41**, 1159–1166.

Clayton, P. J. (1982) Schizoaffective disorders. *Journal of Nervous and Mental Disease*, **170**, 646–650.

Cooley, W. & Lohnes, P. (1971) *Multivariate Data Analysis*. New York: Wiley.

Hirschowitz, J., Zemlan, F. P., Hitzemann, R. J. *et al* (1986) Growth hormone response to apomorphine and diagnosis: a comparison of three diagnostic systems. *Biological Psychiatry*, **21**, 445–454.

Kasanin, J. (1933) The acute schizoaffective psychoses. *American Journal of Psychiatry*, **13**, 97–126.

Kendell, R. E. (1975) *The Role of Diagnosis in Psychiatry*. Oxford: Blackwell.

—— & Gourlay, J. (1970) The clinical distinction between the affective psychoses and schizophrenia. *British Journal of Psychiatry*, **117**, 261–266.

—— & Post, F. (1973) Depressive illness in late life. *British Journal of Psychiatry*, **122**, 615–617.

Kendler, K. S. (1987) The impact of diagnostic misclassification on the pattern of familial aggregation and co-aggregation of psychiatric illness. *Journal of Psychiatric Research*, **21**, 55–91.

Kling, A. S., Metter, J., Riege, W. H., *et al* (1986) Comparison of PET measurement of local brain glucose metabolism and CAT measurement of brain atrophy in chronic schizophrenia and depression. *American Journal of Psychiatry*, **143**, 175–180.

Langfeldt, G. (1939) *The Schizophreniform States*. Copenhagen: Munksgaard.

Leonhard, K. (1957) *Auferlung der Endogen Psychosen*. Jena: Akademie Verlag.

Levinson, D. F. & Levin, M. E. (1987) Schizoaffective mania reconsidered. *American Journal of Psychiatry*, **144**, 415–415.

Meltzer, H. Y., Arora, R. C. & Metz, J. (1984) Biological studies of schizoaffective disorders. *Schizophrenia Bulletin*, **10**, 49–69.

Moran, P. A. P. (1966) The establishment of a psychiatric syndrome. *British Journal of Psychiatry*, **112**, 1165–1171.

Pope, H. G. & Lipinski, J. F. (1978) Diagnosis in schizophrenia and manic–depressive illness: a re-assessment of the specificity of "schizophrenic" symptoms in the light of current research. *Archives of General Psychiatry*, **35**, 811–828.

Radouco-Thomas, S., Garcin, F., Murthy, M. R. V., *et al* (1984) Biological markers in major psychoses and alcoholism: phenotypic and genotypic markers. *Journal of Psychiatric Research*, **18**, 513–539.

Reider, R. O., Mann, L. S., Weinberger, D. R., *et al* (1983) Computed tomographic scans in patients with schizophrenia, schizoaffective and bipolar affective disorder. *Archives of General Psychiatry*, **40**, 735–739.

Shagass, C., Roemer, R. A., Straumanis, J. J., *et al* (1985) Combinations of evoked potential amplitude measurements in relation to psychiatric diagnosis. *Biological Psychiatry*, **20**, 701–722.

Siever, L. J., Coursey, R. D., Alterman, I. S., *et al* (1984) Impaired smooth pursuit eye movement: vulnerability marker for schizotypal personality disorder in a normal volunteer population. *American Journal of Psychiatry*, **141**, 1560–1566.

Stahl, S. M., Woo, D. J., Mefford, I. N., *et al* (1983) Hyperserotonemia and platelet serotonin uptake and release in schizophrenia and affective disorders. *American Journal of Psychiatry*, **140**, 26–30.

Suranyi-Cadotte, B. E., Wood, P. L., Schwartz, G., *et al* (1983) Altered platelet $[^3H]$-imipramine binding in schizoaffective and depressive disorders. *Biological Psychiatry*, **18**, 923–927.

Taylor, M. A. (1984) Schizoaffective and allied disorders. In *Neurobiology of Mood Disorders* (eds R. M. Post & J. C. Ballinger). Baltimore: Williams & Watkins.

Tsai, L. Y., Nasrallah, H. A. & Jacoby, C. G. (1983) Hemispheric asymmetries on computed tomographic scans in schizophrenia and mania: a controlled study and critical review. *Archives of General Psychiatry*, **40**, 1286–1289.

Whalley, L. J., Christie, J. E., Blackwood, D. H. R., *et al* (1989) Disturbed endocrine function in the psychoses: I. Disordered homeostasis or disease process? *British Journal of Psychiatry*, 455–461.

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Consistent Reduction of ACTH responses to stimulation with CRH, Vasopressin and Hypoglycaemia in Patients with Major Depression

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Eleven patients with major depression and 12 control subjects were administered corticotropin-releasing hormone (CRH), aqueous arginine vasopressin (AVP), and insulin hypoglycaemia (IH) to test for differences in hypothalamic–pituitary–adrenal (HPA) axis function. Patients with major depression demonstrated lower ACTH responses to CRH when compared with controls, and a trend toward such after administration of AVP. Despite lower ACTH responses in patients with depression, there were no differences in cortisol responses to these stimuli. In the CRH and AVP tests, there was no correlation between the basal cortisol and ACTH responses in either controls or patients, but in the IH test there was a negative correlation between these responses for both groups. The ACTH responses to CRH and AVP were positively correlated in controls and patients. Cortisol responses to all three provocative stimuli were positively correlated in both subject groups. These findings are consistent with the hypothesis that hypothalamic or supra-hypothalamic overactivity may be involved in the development of HPA-axis abnormalities in patients with depression.

Disturbances in the hypothalamic–pituitary–adrenal (HPA) axis have been demonstrated in patients with major depression by a variety of investigators (Carroll, 1976; Pepper & Krieger, 1984; Kathol, 1985*a*; Reus, 1985). The first of these disturbances to be noted include early escape of cortisol from dexamethasone suppression (Carroll *et al*, 1968, 1981*a*; Carroll, 1972; Schlesser *et al*, 1980; Stokes *et al* 1984; Kocsis *et al*, 1985; Zimmerman *et al* 1986) and elevation of basal plasma (Stokes *et al* 1984; Pfohl *et al*, 1985*a*,*b*; Linkowsky *et al*, 1985) and free cortisol (Carroll, 1972; Carroll *et al*, 1976; Stokes *et al*, 1984; Anton, 1987) in patients with depression when compared with control populations. Studies by Pfohl *et al* (1985*a*,*b*), Linkowski *et al* (1985), and Winokur *et al* (1985) have now also shown higher circadian patterns of adrenocorticotrophic hormone (ACTH) and cortisol levels, especially in dexamethasone suppression test (DST) non-suppressors. Amsterdam *et al* (19883), Gerken & Holsboer (1986) and Jaeckle *et al* (1987) have demonstrated an augmented cortisol response to exogenous ACTH, while Meller *et al* (1987) and Lopez *et al* (1987) have reported similar finding with endogenous ACTH. Other findings from provocative endocrine testing with arginine vasopressin (AVP) (Meller *et al*, 1987), insulin hypoglycaemia (IH) (Lopez *et al*, 1987), and corticotropin-releasing hormone (CRH) (Gold *et al*, 1984, 1986; Gold & Chrousos, 1985; Holsboer *et al*, 1985*a*,*b*; Amsterdam *et al*, 1987) suggest an altered ACTH yet normal cortisol response in patients with depression. Nemeroff *et al* (1984) and Banki *et al* (1987) report elevated cerebrospinal fluid (CSF) CRH levels in patients with depression, while work by Roy *et al* (1987) suggests the same in DST non-suppressors. Finally, there is suggestive evidence that cortisol hypersecretion persists in some even after recovery (Kathol, 1985*b*).

Although plasma cortisol abnormalities have also been identified in other psychiatric conditions (Christie *et al*, 1986), the majority of HPA-axis abnormalities remain most common in patients with depression (Carroll, 1985; Kathol, 1985*a*). Some have even suggested that HPA-axis abnormalities may represent a biological marker for primary affective disorder (Carroll *et al*, 1981*a*). If such is the case, it is important to understand the pathophysiological basis of these abnormalities. With this knowledge it may be possible to identify areas in the central nervous system (CNS) affected by depressive symptoms or, conversely, areas which might be instrumental in predisposing to depressive symptoms.

In order to clarify the levels at which the HPA-axis abnormalities in patients with depression are likely to arise, 11 patients with major depression and 12 control subjects were stimulated with AVP, ovine CRH, and IH on three consecutive days. These three stimuli were chosen since each is known to augment the secretion of ACTH and cortisol by different mechanisms.

Since the identification of ovine CRH (Vale *et al*, 1981), it has been established that AVP and CRH independently possess ACTH-releasing activity (Gibbs, 1986; Antoni, 1986). ACTH and cortisol response to hypoglycaemic stress is thought to be modulated by changes in hypophysiotrophic AVP release, although CRH is a necessary co-factor as it augments the trophic action of AVP (Plotsky *et al*, 1985; Plotsky, 1987).

Although the evidence implicates CRH and vasopressin in the hypoglycaemic ACTH response, maximum plasma ACTH levels after stimulation with CRH or vasopressin or both are less than those which can be achieved during IH (DeBold *et al*, 1984). It is therefore possible that additional factors may be involved in the ACTH response to hypoglycaemia.

By utilising the strategy of performing serial stimulation tests on depressed and control subjects, we were able to compare the pituitary and adrenal response to exogenous centrally acting ACTH stimuli (CRH and AVP) as well as the response to an endogenous ACTH stimulus (IH) which acts at least in part through the influence of CRH and vasopressin. Our results indicate that in patients with depression there is blunting of the ACTH response but not the cortisol response to both CRH and IH, with a trend toward the same findings after AVP. These findings are consistent with the hypothesis that patients with major depression may have down-regulation of both AVP and CRH receptors due to chronic overproduction of vasopressin and CRH and hyper-responsiveness of the adrenal glands to endogenous ACTH.

Method

Subject samples

Twenty-three subjects gave informed consent to participate in a project involving the administration of CRH, AVP, and insulin. Twelve were controls (six males, six females), and eleven were patients in a major depressive episode (three males, six females) or bipolar affective disorder with depression (two females) according to DSM-III (American Psychiatric Association, 1980). Two controls and two patients were post-menopausal. The average age of the controls was 33 years (s.d. 10, range 21–51) and that of the patients was 34 years (s.d. 13, range 21–58).

Control subjects were recruited by advertisement and through a list of people interested in participating in research compiled in the Clinical Research Center. They were screened for the absence of psychiatric disease by a Diagnostic Interview Schedule (DIS); Robins *et al*, 1981) and a standard psychiatric interview. None had other medical conditions or were on medication. Prior to inclusion all were documented to have a normal physical examination, normal blood count, and normal blood-chemistry screen.

Patients with depression were recruited from the in-patient psychiatry service at the University of Iowa Hospitals. All had documented major depression, as determined by the DIS and a standard clinical interview. Utilising Research Diagnostic Criteria (RDC; Spiter *et al*, 1978), eight had major depressive disorder while three met criteria for schizoaffective disorder, depressed type (two were bipolar according to DSM-III). None had other Axis I diagnoses from DSM-III or antisocial personality disorder. None of the patients had a medical condition or were on medications known to interfere with the provocative endocrine tests employed. However, ten of the eleven patients were on psychotropic medications at the time of testing. There were five on antipsychotic medication, six on tricyclic antidepressants, four on benzodiazepines, three on lithium, and two on carbamazepine. Seven of the ten were on a drug combination. During the three days of endocrine testing, the patients were maintained on a constant dose of the medication(s) which they had been taking at admission, to avoid activation of the HPA axis by drug withdrawal (Dilsaver & Greden, 1984; Devanand *et al*, 1984; Kraus *et al*, 1987).

All participants were tested on the Hamilton Rating Scale for Depression (HRSD; Hamilton, 1960) and Carroll Rating Scale for Depression (CRSD; Carroll *et al*, 1981*b*) on entry into the study. The mean score of the controls differed significantly ($P<0.0001$) from that of the patient on both the CRSD (2 (s.e. 1) and 32 (s.e. 2) respectively) and the HRSD (2 (s.e. 0.5) and 20 (s.e. 2) respectively). All patients had HRSD scores greater than 13, and all CRSD scores were greater than 17.

Endocrine testing procedures

After initial clinical screening for depression, patients, who signed informed consents, were given the DIS, HRSD, and CRSD. A physical examination was performed, and laboratory testing (including thyroid-function tests) was completed during the patient's first or second day in hospital. If no exclusion criteria were identified, the patients were accompanied to the Clinical Research Center at 14.45 h on the three succeeding days. At 15.00 h each day a butterfly catheter was inserted, and at 16.00 h (a time of relatively stable ACTH and cortisol secretion) the following testing procedures were performed. On day 1, 4.15 nmol (0.18 International pressor units)/kg of aqueous AVP was administered intramuscularly. On day 2, 1.0 μg/kg of ovine CRH, and on day 3, 0.15 units/kg of regular purified pork insulin, was administered over 15–30 seconds intravenously. Patients did not eat for four hours prior to testing, and remained supine and fasted throughout each test. During each test, blood samples were obtained for determination of plasma ACTH and cortisol levels at 0, 5, 10, 15, 30, 45, 60, 75, 90, 120, 150, and 180 minutes. Blood samples were collected in pre-chilled tubes, placed in ice, and spun in a refrigerated centrifuge within an hour of collection. Plasma was then divided and stored in vials at −20 C until assay.

Ovine CRH was obtained through Dr Stanley Watson at the University of Michigan, who prepared material obtained from Dr Wylie Vale of the Salk Institute for human administration. The purity of the ovine CRH used in this project has been previously established (Vale *et al*, 1981; Rivier *et al*, 1982). It was administered through a short plastic tube from a plastic syringe, both pre-coated with buffer to control for loss through leaching on to the plastic surfaces. Using this technique, Dr Watson has demonstrated that ovine CRH can be administered in concentrations as low as 0.03 μg/kg and still achieve consistent plasma levels of ovine CRH in humans (Lopez *et al*, 1984).

On day 5 all patients had a 1 mg dexamethasone suppression test (DST) as previously described (Jaeckle *et al*, 1987). Three of the patients included in the project were DST non-suppressors; however, two of these were on carbamazepine, which is known to interfere with dexamethasone metabolism (Privitera *et al*, 1982). Thus only one patient can be called a DST non-suppressor. For this reason, categorisation according to DST suppressor/non-suppressor status will not be done.

Control subjects had a history, physical examination, and laboratory screen and were given the DIS, HRSD, and CRSD prior to admission into the study. Those meeting criteria for inclusion were given the stimulation tests in the Clinical Research Center, as described for patients.

After injection of CRH, AVP, and insulin, the occurrence of side-effects was monitored at each blood-sampling period. With CRH administration, one patient and two controls experienced brief facial flushing, and one agitated depressed patient became more restless five minutes after the CRH was given. Other minor side-effects (tingling, warmth, metallic taste, and dizziness) were transient, rare, and experienced equally by both depressed and control subjects. After AVP administration, mild, transient gastrointestinal sensations, and facial pallor noticed only by an external observer, were found in a small but equal number of controls and patients. Insulin-induced hypoglycaemia caused an adrenergic response (sweating, tachycardia, weakness, hunger, and/or tremor) in all subjects. These symptoms were tolerated well and required termination of the test in none.

Only eight of the patients completed the IH test. Of the three patients who did not complete it, one was excluded because of failure to achieve adequate hypoglycaemia (<40 mg/dl), and two refused. All three were on psychotropic medication, and one of the three carried a diagnosis of schizoaffective disorder, depressed type, according to RDC criteria.

Laboratory methods

In this study, ACTH was measured by two assays using different ACTH trace and antibody. This was done because the Medical Research Facility Laboratory was forced to change the source of trace and antibody midway into the study. The majority of the samples (12 controls, 6 patients) were assayed by a method which utilised an antibody and trace resulting in higher basal and stimulated levels of ACTH and less sensitivity (10 pg/ml v. 5 pg/ml) than the new assay. The old assay has been previously described (Pfohl *et al*, 1985*b*). The new assay utilised an antibody obtained from IgG corporation, Nashville, Tennessee, and a trace from Radioimmunoassay System Laboratory, Carson, California. Other techniques of the assay remained the same. Correlation of plasma ACTH levels from the two assays was extremely high ($r = 0.962$; $r^2 = 0.926$; $P < 0.001$) when comparable control samples were measured before and after the assay change. The intra-assay coefficients of variation (CVs) for the old assay were 7.1%, 5.5%, and 4.8% for ACTH concentrations of 10 mg/ml, 59 pg/ml, and 408 pg/ml respectively. The corresponding inter-assay CVs were 6.2%, 12.4%, and 11.5% respectively. For the new assay the intra-assay CVs were 10.0% and 4.1% for ACTH concentrations of 9 pg/ml and 82 pg/ml respectively. Corresponding inter-assay CVs for the new assay were 9.0% and 6.9% respectively. Low controls were uniformly undetectable. All samples from the same subject were run in the same assay by a technician blind to the clinical diagnosis. In order to compare results from the two assays, the regression line from the above correlation was used to predict new assay values from the old assay levels. This was considered the more conservative means of normalising the ACTH levels, since this conversion tended to bring patient and control values closer together, thus decreasing the likelihood of finding differences between groups. When patients who had ACTH levels measured with the old assay were compared with those who had ACTH levels measured with the new assay, there were no differences for the CRH test or the AVP test between groups. For the IH test, however, patients whose ACTH levels were measured with the old assay had significantly lower levels at 45 and 60 minutes (these were times when the limits of the assay were stretched).

The cortisol assay has been previously described in detail (Pfohl *et al*, 1985*b*; Lopez *et al*, 1987). The sensitivity of the radioimmunoassay for cortisol in unextracted serum was 0.5 μg/dl. The intra-assay CVs were 9.3%, 9.6%, and 8.5% at serum cortisol concentrations of 2.7 μg/dl, 11.7 μg/dl, and 23.6 μg/dl respectively. The corresponding inter-assay CVs were 12.7%, 9.1%, and 10.9%. All samples from the same subject were run in the same assay by a technician blind to the clinical diagnosis.

Data analysis

ACTH and cortisol responses to each of the provocative hormonal stimuli were compared as a two-factor experiment (group and time), with repeated measures on one factor (time). Hence, a two-way repeated-measures analysis of variance (ANOVA) was performed on the data (Winer, 1971). When appropriate, the data were re-analysed by analysis of covariance while controlling for basal plasma ACTH and cortisol concentrations. The net integrated area under the hormone response curve (the total area under the line defining the individual response but above the basal concentrations) was calculated using the trapezoid method for each subject, and the means for the groups were compared using student's *t*-test (Snedecor & Cochran, 1980). The gross integrated area under the response curve (the total area under the curve defining the individual response regardless of baseline) was also calculated, as a reflection of the total plasma hormone pool, and the means for the groups were compared using Student's *t*-test.

As a means of assessing the cortisol feedback mechanism, log basal ACTH and log ACTH response after each of the provocative stimuli were correlated with basal serum cortisol levels for that test using the Pearson correlation coefficient (Snedecor & Cochran, 1980). The log of ACTH was used, since ACTH bears a log/linear relationship to cortisol (Keller-Wood & Dallman, 1984). The ratios of net and gross stimulated cortisol to net and gross stimulated log ACTH (net cortisol/log net ACTH, gross cortisol/log gross ACTH) were calculated to assess the cortisol responsiveness to a given amount of ACTH. The mean ratios for the groups were compared utilising Student's *t*-test. To assess the consistency of hormonal responses across the three tests, pair-wise Pearson correlations between the net ACTH, gross ACTH and cortisol responses were calculated. The Bonferroni test (Snedecor & Cochran, 1980) was used to correct for the number of correlations performed.

Results

Arginine vasopressin test

Both patients and control subjects had significant increments in ACTH ($F=32.8$, d.f. $=11$, $P<0.0001$) and cortisol ($F=22.6$, d.f. $=11$, $P<0.0001$) levels after stimulation with AVP. The analysis of the group-by-time interaction did not demonstrate a significant time-dependent difference between groups. When the net integrated areas under the ACTH and cortisol response curves were compared, no difference could be identified ($t=1.9$, d.f. $=21$, $P=0.07$) (Fig. 1).

Corticotropin-releasing hormone test

Both patients and control subjects demonstrated a rise in ACTH ($F=22.2$, d.f. $=11$, $P<0.0001$) and cortisol ($F=44.2$, d.f. $=11$, $P<0.0001$) levels after stimulation with ovine CRH (Fig. 2). Analysis of the group-by-time interaction reveals that patients had significantly lower ACTH levels than controls (Fig. 2). Significant group differences, however, were lost when adjustments were made by covarying for basal ACTH concentrations. When the ACTH responses were compared by measurement of the net integrated area under the response curve (Fig. 1), patients were found to have a blunted ACTH response ($t=2.4$, d.f. $=21$, $P=0.02$). Net and gross integrated cortisol responses to ovine CRH did not show any difference between groups nor any trend toward such (Fig. 2).

Insulin-induced hypoglycaemia

Plasma glucose decrease after insulin administration (Fig. 3) was comparable between groups ($F=2.3$, $P=0.15$). The mean glucose nadir for patients was 29.0 (s.e. 2.2) mg/dl, while that for controls was 27.6 (s.e. 1.5) mg/dl. All participants reached nadir glucose levels of 40 mg/dl or less. When analysed for a group-by-time interaction, patients were found to have a significantly more rapid return of glucose levels toward baseline than controls at 75, 90 and 120 minutes (Fig. 3), although all subjects returned to baseline levels by 180 minutes.

Both patients and control subjects had significant ACTH and cortisol responses to the IH ($P<0.0001$) (Fig. 4). An appropriate sequence of response was also identified, with the glucose nadir occurring at 30 minutes, the ACTH peak at 45 minutes, and the cortisol peak at 75–90 minutes. When analysed for the group-by-time interaction, patients had significantly lower ACTH responses to IH than control

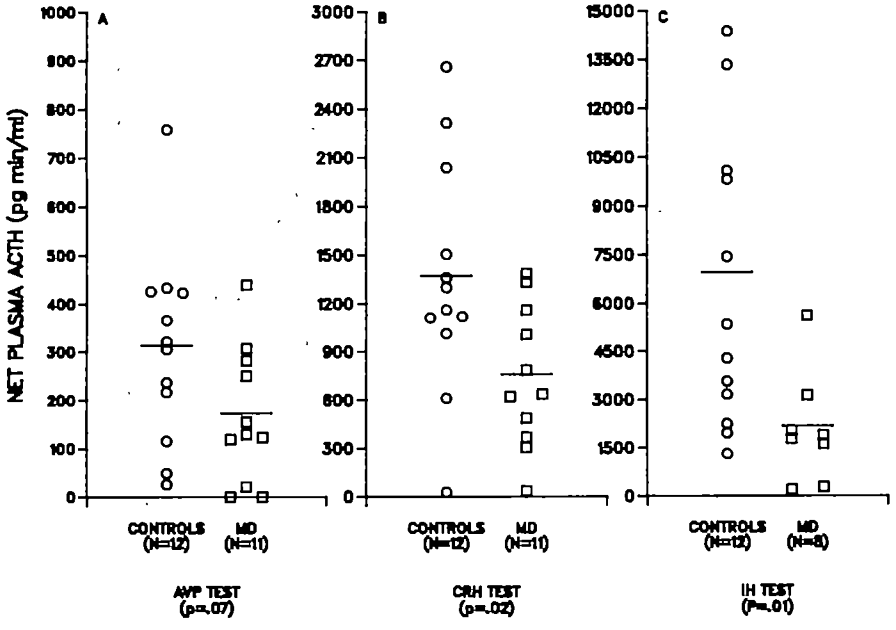

FIG. 1 Net integrated areas under the ACTH curves for patients with major depression (MD) and controls: AVP, CRH and IH tests.

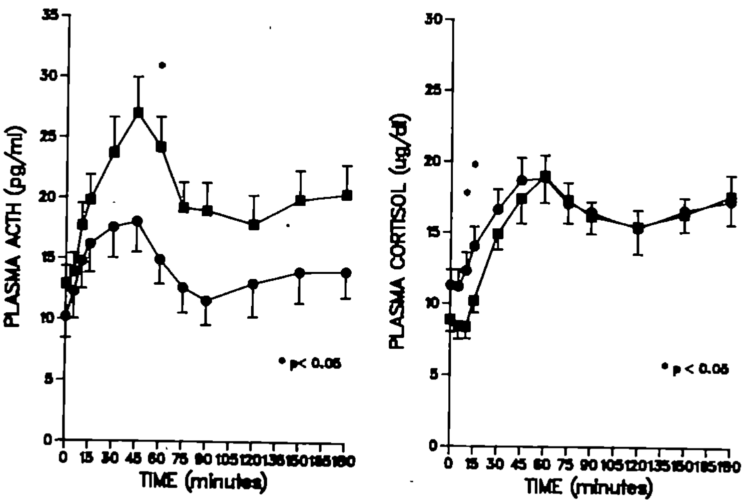

FIG. 2 Plasma ACTH and cortisol responses to CRH: ● patients; ■ controls.

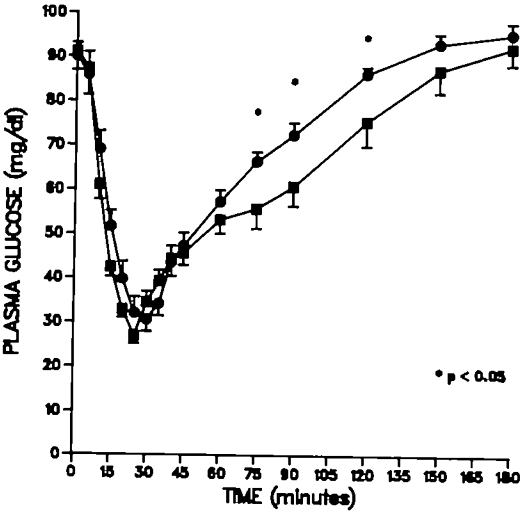

FIG. 3 Plasma glucose after insulin injection: ● patients; ■ controls.

subjects (Fig. 4). When the two groups were compared using the net integrated area under the ACTH response curve, patients had blunted ACTH responses ($t=3.0$, d.f. $=15.2$, $P=0.01$ (Fig. 1).

Since there was a change in the ACTH assay mid-study and there was a significant difference at 45 and 60 minutes between old and new ACTH assay results for the patients, a further comparison was made which included only those controls and patients whose ACTH was measured by the old assay. In this subgroup, patients with depression still tended to have lower ACTH response ($F=4.19$, d.f. $=1$, $P=0.06$).

Evaluation of the group-by-time interaction for the cortisol response to IH revealed that controls had higher plasma cortisol levels, but only late in the response curve (Fig. 4). The net integrated cortisol response to IH was significantly greater in control subjects than in patients ($t=2.3$, d.f. $=18$, $P=0.03$).

Relationship of basal ACTH levels and net integrated ACTH to basal and stimulated cortisol levels

The correlation of basal cortisol to log basal ACTH before AVP, CRH, and IH administration was insignificant in both controls and patients. There was, however, a significant negative correlation of basal cortisol to log gross ACTH response during IH for patients ($r=-0.70$, $P=0.05$) and for control subjects ($r=-0.60$, $P=0.04$) (Table I). No such negative correlation was found for the CRH and AVP tests. Table II shows, for each of the stimulation tests, the ratio of the gross area under the cortisol response curve to the log of the gross area under the ACTH response curve, and the corresponding ratio for the net areas. Although no individual differences between groups can be found in the ratios for each test, the ratio of gross cortisol response to log gross ACTH response is consistently higher in the patients than in the controls. Such is not found for the net cortisol response.

Correlation of ACTH and cortisol responses between tests

There were no significant correlations between the net ACTH responses to CRH, AVP and IH in control subjects (Table III). There was, however, a significant positive correlation between the net ACTH responses to AVP and CRH in patients ($r=0.79$, $P=0.004$). A significant positive correlation was also found in the gross ACTH responses to AVP and CRH in control subjects ($r=0.92$, $P=0.0001$),

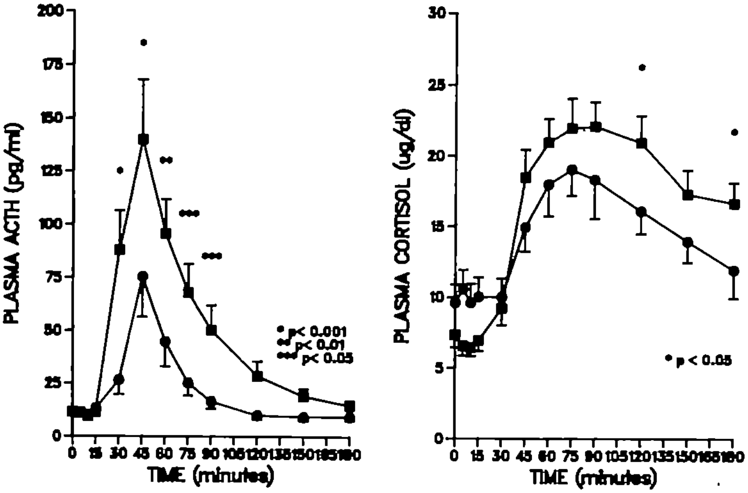

FIG. 4 Plasma ACTH and cortisol responses to IH: ● patients; ■ controls.

TABLE I

Correlations of baseline cortisol with gross area under the ACTH response curve, and net area under the ACTH response curve for the CRH, AVP and IH tests

		CRH			*AVP*			*IH*	
	n	r	P	n	r	P	n	r	P
Log_{10} gross area ACTH									
Controls	12	0.475	0.119	12	−0.227	0.477	12	−0.602	0.038
Patients	11	−0.021	0.950	11	0.006	0.999	8	−0.698	0.054
All	23	−0.010	0.962	23	−0.188	0.390	20	−0.676	0.001
Log_{10} net area ACTH									
Controls	12	0.257	0.420	12	0.153	0.636	12	−0.598	0.040
Patients	11	−0.047	0.890	11	0.387	0.303	8	−0.509	0.197
All	23	0.117	0.691	23	0.185	0.423	20	−0.614	0.004

TABLE II

Adrenal response to endogenous ACTH, as measured by the ratio of gross cortisol production to log gross ACTH production, and by the ratio of net cortisol production to log net ACTH production

	Controls				*Patients*			
	Ratio (gross)		*Ratio (net)*		*Ratio (gross)*		*Ratio (net)*	
	Mean	*(s.e. mean)*	*Mean*	*(s.e. mean)*	*Mean*	*(s.e. mean)*	*Mean*	*(s.e. mean)*
CRH test (12 controls, 11 patients)	797	54	449	86	897	91	378	82
AVP test (12 controls, 11 patients)	556	45	163	40	677	59	421	212
IH test (12 controls, 8 patients)	719	73	438	54	753	94	299	52

TABLE III

Correlations between net and gross ACTH responses and CRH, AVP, and IH in patients, control subjects, and in the total group tested

	Controls		*Patients*		*All*	
	r	P	r	P	r	P
Net ACTH response						
CRH:IH	−0.12	0.70	−0.27	0.52	0.08	0.74
CRH:AVP	−0.22	0.48	0.79	0.004	0.22	0.29
AVP:IH	−0.04	0.91	−0.04	0.92	0.14	0.55
Gross ACTH response						
CRH:IH	0.04	0.91	0.42	0.30	0.24	0.30
CRH:AVP	0.92	0.0001	0.94	0.0001	0.94	0.0001
AVP:IH	−0.04	0.89	0.41	0.32	0.21	0.37

TABLE IV

Correlations between the gross cortisol responses to CRH, VP and IH in patients, control subjects, and the total group tested

	Controls		*Patients*		*All*	
	r	P	r	P	r	P
CRH:IH	0.76	0.004	0.75	0.03	0.72	0.0003
CRH:AVP	0.67	0.016	0.72	0.01	0.70	0.0002
AVP:IH	0.79	0.002	0.56	0.15	0.65	0.0010

in patients ($r = 0.94$, $P < 0.0001$) and in the group taken as a whole ($r = 0.94$, $P < 0.001$) (Table III). Neither net nor gross ACTH responses to IH were correlated with those to CRH or AVP.

No significant relationships were found in the net cortisol responses to CRH, AVP and IH in control subjects or patients, but there was a significant positive correlation between the net cortisol responses to IH and CRH when the two groups were pooled ($r = 0.64$, $P = 0.003$). For the gross cortisol response, however, significant positive correlations were seen in nearly all comparisons between tests (Table IV).

Discussion

The purpose of this study was to determine the effects of CRH, AVP, and insulin (which presumably increases ACTH and cortisol secretion through the release of endogenous CRH and/or AVP) on the secretion of ACTH and cortisol in patients with major depression. The major finding is that there is a consistent reduction in net ACTH production (albeit marginal with AVP) in response to these three provocative stimuli in patients with major depression when compared with a control population. In fact, the patients who had the least ACTH response to AVP were the same that had the least response to CRH. Such was not the case in control subjects.

Other investigators have reported that the ACTH response to CRH is blunted in patients with major depression when compared with control populations and patients with Cushing's disease (Gold *et al*, 1984, 1986; Gold & Chrousos, 1985; Holsboer *et al*, 1985*a*,*b*; Amsterdam *et al*, 1987). It has been suggested that this is the result of negative-feedback inhibition by cortisol of ACTH secretion (Gold *et al*, 1987); the suggestion being supported by the fact that basal cortisol levels are inversely correlated with the ACTH response to this challenge (Gold *et al*, 1984, 1986; Gold & Chrousos, 1985; Holsboer *et al*, 1985*b*, 1986). Not all investigators, however, have identified this relationship in those patients with a blunted ACTH response to CRH (Holsboer *et al* 1985*a*; Amsterdam *et al*, 1987). The results from the small number of patients reported here would suggest that other factors may be involved in this finding, although a type II statistical error cannot be excluded.

Few investigators have measured ACTH levels in depressed patients after stimulation with AVP or insulin. AVP is a less potent ACTH secretogogue than CRH in man, and has not been studied in much depth, because in its early form (lysine vasopressin) innate secretory potential could not be separated from secretion stimulated by the stress response associated with its administration. Use of arginine vasopressin has bypassed this problem (as is illustrated by the few side-effects experienced by the patients in our study) and allowed the assessment of an alternative ACTH secretogogue to be used in this population. In this preliminary study the ACTH response is probably physiologically blunted, since it occurs in the same predicted direction as seen with CRH. The difference, however, is not statistically discernible in the present experiment. The ACTH response to AVP in our patients does correlate with the response to CRH in the same patients.

The exact mechanism by which insulin acts in initiating the secretion of ACTH is not known. Current hypotheses discussed in the introduction suggest that both AVP and CRH are involved in the secretory process (Plotsky, 1987). If these two peptides are critical components to hypoglycaemia-induced ACTH secretion in man, then our findings are consistent with those reported with the administration of exogenous AVP and CRH (i.e. a decrease in ACTH responsivity).

Cortisol production essentially did not differ between groups despite a decrease in ACTH response in those with major depression. This is most evident with the AVP and CRH tests, in which depressed patients had non-significantly greater net and gross cortisol production, despite reduced ACTH response. On the other hand, with insulin, controls had a greater net cortisol production than patients.

The comparable secretion of cortisol between controls and patients after AVP and CRH administration would suggest that patients with depression have an augmented cortisol response to endogenous ACTH. Such has been reported with exogenous ACTH (Amsterdam *et al*, 1983; Gerken & Holsboer, 1986; Jaeckle *et al*, 1987) and inferred with endogenous ACTH (Meller *et al*, 1987; Lopez *et al*, 1987) in patients with major depression by several investigators. Greater production of cortisol in controls after insulin, and a higher net cortisol to log net ACTH production after insulin and CRH, however, suggest the opposite in our small subset of patients. It is only when the gross cortisol to log gross ACTH production is calculated that a trend to increased adrenal sensitivity is found. This suggests that it is not only the increment in ACTH level which affects the amount of cortisol production, but also the degree of basal secretion on to which the stimulated increase occurs.

The findings in this study are consistent with the hypothesis that hypothalamic–pituitary–adrenal axis changes identified in patients with major depression are the result of hypothalamic or supra-hypothalamic overdrive. Reduced ACTH production in response to the three provocative stimuli in this study could be due to chronic hypersecretion of CRH and AVP, with down-regulation of both CRH and AVP receptors. This is consistent with basic work performed by several investigators (Reisine & Hoffman, 1983; Wynn *et al*, 1985), who have shown that CRH receptor down-regulation is what happens when chronic CRH is given in the animal model. Such a hypothesis is also consistent with other findings in patients with depression. One would expect high basal plasma and urinary cortisol production, dexamethasone non-suppression, elevated circadian secretion of ACTH and cortisol, augmented cortisol response to ACTH, and increased cerebrospinal fluid (CSF) CRH levels. All of these are well documented in the subset of patients with depression, with the exception of elevated CSF CRH levels. There have been two studies showing elevated levels of CSF CRH in patients with depression (Nemeroff *et al*, 1984; Banki *et al*, 1987), and one study in which no such elevation was found (Roy *et al*, 1987). However, in the study showing no elevation in level, patients with dexamethasone non-suppression showed a trend in the predicted direction (Roy *et al*, 1987).

Several problems in the present study limit acceptance of the conclusion without reservations. First, the number studied is small. Second, the majority of patients were dexamethasone suppressors. Third, there was an unfortunate ACTH assay change during the course of the study. Fourth, there were possible carry-over effects from one part of the study to the next, since only one day separated successive tests. And fifth, the patients were on medication.

The fact that we have found significant differences in such a small number of patients consistently among the three tests, especially as the patients were in large part suppressors at the time of testing, would tend to bolster the robustness of our findings.

Given the unavoidable circumstances resulting in a change in the ACTH assay toward the end of the study period, we attempted to correlate results between the old and new assay in the most conservative way possible. Although this change necessarily introduces another source of variance into our results, the results remain consistent from test to test in the sample as a whole.

Despite the fact that early tests could have influenced the results of tests performed during the latter part of the study, they would have done so in both controls and patients. The differences between groups therefore remain real even if a carry-over effect was taking place.

The majority of patients in this study were on fixed doses of medication. Although we were able to obviate the effect of medication withdrawal on our results, it is still possible that the medications the patients were taking could have influenced the findings. A recent evaluation of the ACTH and cortisol responses to AVP before and after imipramine does not suggest that this medication interferes with test results (Wysham *et al*, 1986). Whether other medications show a similar lack of effect on the AVP test has not been studied.

To date, our laboratory has not performed CRH testing before and after the administration of therapeutic doses of psychotropic medications. Since our results concur with the findings of Gold *et al* (1984, 1986), Gold & Chrousos (1985), Holsboer *et al* (1985*a*,*b*) and Amsterdam *et al* (1987), who studied drug-free patients, it makes it less likely that medication alters the ACTH response to CRH. Furthermore, Holsboer *et al* (1985*a*) performed serial CRH stimulation tests on patients recovering from depression and found that changes occurred in relationship to clinical status rather than medication adjustment.

The insulin tolerance test could also be influenced by medication effects. In a study of 18 patients with major depression, Lopez *et al* (1987) were unable to find a difference in ACTH response to IH testing between those on and off various psychotropic medications. Nonetheless, most of the patients in that study were on medication. Holl *et al* (1986) also noted little effect of acute administration of desipramine and clomipramine on pre- and post-test results. Our research team is currently investigating the effect of imipramine on ACTH and cortisol responses to IH. In the 14 subjects tested thus far, no significant differences have been found.

The above discussion has focused on the implications of our results on the pathophysiology of cortisol abnormalities in patients with depression, without addressing their aetiological relationship to the depressive syndrome. Although current evidence suggests that there is an abnormality in the hypothalamic/limbic driving force of the pituitary–adrenal axis which may be mediated by CRH and/or vasopressin, this abnormality may be only indirectly related to the behavioural syndrome. The theories of aetiology of HPA-axis changes in patients with major depression continue to be protean and include such things as (a) stress (Mellsop *et al*, 1985), (b) appetite and weight (Edelstein *et al*, 1983; Zimmerman *et al*, 1984; Keitner *et al*, 1985; Krishnan *et al*, 1985; Fichter & Pirke, 1986; Pfohl *et al*, 1986; Mullen *et al*, 1986), (c) age (Asnis *et al*, 1981; Oxenkrug *et al*, 1983; Lewis *et al*, 1984; Nelson *et al*, 1984; Rosenbaum *et al*, 1984; Greden *et al*, 1986), and (d) behavioural syndrome itself (Carroll, 1985).

An additional and intriguing hypothesis about HPA-axis abnormalities in patients with depression is that they are in some way related to the development of depressive symptomatology: they are the cause of what some clinicians like to call a 'biological depression'. Even in this situation it cannot be stated with certainty that the direct cause of the symptoms is the proposed central hypothalamic/limbic defect, since hypercortisolemia itself could be more closely related to the development of symptoms. After all, patients with primary adrenal and pituitary-dependent Cushing's disease have a high yet equal incidence of depressive symptomatology, and these symptoms subside with treatment of the hypercortisolemia alone (Kathol, 1985*a*).

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References

AMERICAN PSYCHIATRIC ASSOCIATION, COMMITTEE ON NOMENCLATURE AND STATISTICS (1980) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn). Washington DC: American Psychiatric Association.

AMSTERDAM, J. D., WINOKUR, A., ABELMAN, E., *et al* (1983) Cosyntropin (ACTH$_{\text{alpha 124}}$) stimulation test in depressed patients and healthy subjects. *American Journal of Psychiatry*, **140**, 907–909.

——, MAISLIN, G., WINOKUR, A., *et al* (1987) Pituitary and adrenocortical responses to the ovine corticotropin releasing hormone in depressed patients and healthy volunteers. *Archives of General Psychiatry*, **44**, 775–781.

ANTON, R. F. (1987) Urinary free cortisol in psychotic depression. *Biological Psychiatry*, **22**, 24–34.

ANTONI, F. A. (1986) Hypothalamic control of adrenocorticotropin secretion: advances since the discovery of 41-residue corticotropin-releasing factor. *Endocrine Reviews*, **7**, 351–378.

ASNIS, G. M, SACHAR, E. J., HALBREICH, U., *et al* (1981) Cortisol secretion in relation to age in major depression. *Psychosomatic Medicine*, **43**, 235–242.

BANKI, C. M., BISSETTE, G., ARATO, M., *et al* (1987) CSF corticotropin-releasing factor-like immunoreactivity in depression and schizophrenia. *American Journal of Psychiatry*, **144**, 873–877.

CARROLL, B. J. (1972) Control of plasma cortisol levels in depression: studies with the dexamethasone suppression test. In *Depressive Illness: Some Research Studies* (eds B. Davies, B. J. Carroll & R. M. Mowbray). Springfield, Illinois: Charles C. Thomas.

—— (1976) Psychoendocrine relationships in affective disorders. *Modern Trends in Psychosomatic Medicine*, **3**, 121–153.

—— (1985) Dexamethasone suppression test: a review of contemporary confusion. *Journal of Clinical Psychiatry*, **46**, 13–24.

——, Martin, F. I. R. & Davies, B. (1968) Resistance to suppression by dexamethasone of plasma 11-O.H.C.S. levels in severe depressive illness. *British Medical Journal*, *iii*, 285–287.

——, Curtis, G. L., Davies, B. M., *et al* (1976) Urinary free cortisol excretion in depression. *Psychological Medicine*, **6**, 43–50.

——, Feinberg, M., Greden, J. F., *et al* (1981*a*) A specific laboratory test for the diagnosis of melancholia. *Archives of General Psychiatry*, **38**, 15–22.

——, ——, Smouse, P. E., *et al* (1982*b*) The Carroll Rating Scale for Depression: development, reliability, and validation. *British Journal of Psychiatry*, **138**, 194–200.

Christie, J. E., Whalley, L. J., Dick, H., *et al* (1986) Raised plasma cortisol concentrations a feature of drug-free psychotics and not specific for depression. *British Journal of Psychiatry*, **148**, 58–65.

DeBold, C. R., Sheldon, W. R., DeCherney, G. S., *et al* (1984) Arginine vasopressin potentiates adrenocorticotropin release induced by ovine corticotropin-releasing factor. *Journal of Clinical Investigation*, **73**, 533–538.

Devanand, D. P., Pandurangi, A. K. & Dewan, M. J. (1984) False-positive dexamethasone suppression test results related to antipsychotic drug withdrawal: case report. *Clinical Psychiatry*, **45**, 275–276.

Dilsaver, S. C. & Greden, J. F. (1984) Effects of antidepressant withdrawal on the dexamethasone suppression test. *Psychiatry Research*, **14**, 111–122.

Edelstein, C. K., Roy-Byrne, P., Fawzy, F. I., *et al* (1983) Effects of weight loss on the dexamethasone suppression test. *American Journal of Psychiatry*, **140**, 338–341.

Fichter, M. M. & Pirke, K. M. (1986) Effect of experimental and pathological weight loss upon the hypothalamo–pituitary–adrenal axis. *Psychoneuroendocrinology*, **11**, 295–305.

Gerken, A. & Holsboer, F. (1986) Cortisol and corticosterone response after syn-corticotropin in relationship to dexamethasone suppressibility of cortisol. *Psychoneuroendocrinology*, **11**, 185–194.

Gibbs, D. M. (1986) Vasopressin and oxytocin: hypothalamic modulators of the stress response: a review. *Psychoneuroendocrinology*, **11**, 131–140.

Gold, P. W., Chrousos, G. P., Kellner, C., *et al* (1984) Psychiatric implications of basic and clinical studies with corticotropin-releasing factor. *American Journal of Psychiatry*, **141**, 619–627.

—— & —— (1985) Clinical studies with corticotropin releasing factor: implications for the diagnosis and pathophysiology of depression, Cushing's disease, and adrenal insufficiency. *Psychoneuroendocrinology*, **10**, 401–419.

——, Loriaux, D. L., Roy, A., *et al* (1986) Responses to corticotropin-releasing hormone in the hypercortisolism of depression and Cushing's disease. *New England Journal of Medicine*, **314**, 1329–1336.

——, Kling, M. A., Khan, I., *et al* (1987) Corticotropin releasing hormone: relevance to normal physiology and to the pathophysiology and differential diagnosis of hypercortisolism and adrenal insufficiency. In *Hypothalamic Dysfunction in Neuropsychiatric Disorders* (eds D. Nerozzi, F. K. Goodwin & E. Costa). New York: Raven Press.

Greden, J. F., Flegel, P., Haskett, R., *et al* (1986) Age effects in serial hypothalamic–pituitary–adrenal monitoring. *Psychoneuroendocrinology*, **11**, 195–204.

Hamilton, M. (1960) A rating scale for depression. *Journal of Neurology, Neurosurgery, and Psychiatry*, **23**, 56–72.

Holl, W. R., Fehm, H. L., Voigt, K. H., *et al* (1986) Acute effects of desipramine and clomipramine on pituitary–adrenal axis in man. *Hormone and Metabolism Research*, **18**, 134–137.

Holsboer, F., Gerken, A., Stalla, G. K., *et al* (1985*a*) ACTH, cortisol, and corticosterone output after ovine corticotropin-releasing factor challenging during depression and after recovery. *Biological Psychiatry*, **20**, 276–286.

——, ——, Stalla, G. K., *et al* (1985*b*) Blunted corticotropin and normal cortisol response to human corticotropin-releasing factor in depression. *New England Journal of Medicine*, **311**, 1127.

——, ——, Von Bardeleben, U., *et al* (1986) Human corticotropin-releasing hormone in depression–correlation with thyrotropin secretion following thyrotropin-releasing hormone. *Biological Psychiatry*, **21**, 601–611.

Jaeckle, R. S., Kathol, R. G., Lopez, J. F., *et al* (1987) Enhanced adrenal sensitivity to exogenous ACTH$_{\text{alpha 1-24}}$ stimulation in major depression: relationship to dexamethasone suppression test result. *Archives of General Psychiatry*, **43**, 233–240.

Kathol, R. G. (1985*a*) Etiologic implications of corticosteroid changes in affective disorder. *Psychiatric Medicine*, **3**, 135–162.

—— (1985*b*) Persistent elevation of urinary free cortisol and loss of circannual periodicity in recovered depressive patients. *Journal of Affective Disorders*, **8**, 137–145.

Keitner, G. I., Brown, W. A., Qualls, C. B., *et al* (1985) Results of the dexamethasone suppression test in psychiatric patients with and without weight loss. *American Journal of Psychiatry*, **142**, 246–247.

Keller-Wood, M. E. & Dallman, M. F. (1984) Corticosteroid inhibition of ACTH secretion. *Endocrine Reviews*, **5**, 1–24.

Kocsis, J. H., Davis, J. M., Katz, M. M., *et al* (1985) Depressive behavior and hyperactive adrenocortical function. *American Journal of Psychiatry*, **142**, 1291–1298.

Kraus, R. P., Hux, M. & Grof, P. (1987) Psychotropic drug withdrawal and the dexamethasone suppression test. *American Journal of Psychiatry*, **144**, 82–85.

Krishnan, K. R. R., France, R. D., Snipes, M. T., *et al* (1985) Weight change and the dexamethasone suppression test. *Biological Psychiatry*, **20**, 1015–1018.

Lewis, D. A., Pfohl, B., Schlechte, J., *et al* (1984) Influence of age on the cortisol response to dexamethasone. *Psychiatry Research*, **13**, 213–220.

Linkowski, P., Mendlewicz, J., Leclercq, R., *et al* (1985) The 24-hour profile of adrenocorticotropin and cortisol in major depressive illness. *Journal of Clinical Endocrinology and Metabolism*, **61**, 429–438.

Lopez, J. F., Watson, S., Young, E., *et al* (1984) CRF releases beta-endorphin/beta-LPH in normal humans. *Society of Neuroscience Abstracts*, **10**, 83.

——, Kathol, R. G., Jaeckle, R. S., *et al* (1987) The HPA axis response to insulin hypoglycemia in depression. *Biological Psychiatry*, **22**, 153–166.

Meller, W. H., Kathol, R. G., Jaeckle, R. S., *et al* (1987) Stimulation of the pituitary–adrenal axis with arginine vasopressin in patients with depression. *Psychiatric Research*, **21**, 269–277.

Mellsop, G. W., Hutton, J. D. & Delahunt, J. W. (1985) Dexamethasone suppression test as a simple measure of stress? *British Medical Journal*, **290**, 1804–1806.

Mullen, P. E., Linsell, C. R. & Parker, D. (1986) Influence of sleep disruption and calorie restriction on biological markers for depression. *Lancet*, *ii*, 1051–1055.

Nelson, W. H., Orr, W. W., jr, Shane, S. R., *et al* (1984) Hypothalamic–pituitary–adrenal axis activity and age in major depression. *Clinical Psychiatry*, **45**, 120–121.

Nemeroff, C. B., Widerlov, E., Bissette, G., *et al* (1984) Elevated concentrations of CSF corticotropin-releasing factor-like immunoreactivity in depressed patients. *Science*, **226**, 1342–1344.

Oxenkrug, G. F., Pomara, N., McIntyre, I. M., *et al* (1983) Aging and cortisol resistance to suppression by dexamethasone: a positive correlation. *Psychiatry Research*, **10**, 125–130.

Pepper, G. M. & Krieger, D. T. (1984) Hypothalamic–pituitary–adrenal abnormalities in depression: their possible relation to central mechanisms regulating ACTH release. In *Neurobiology of Mood Disorders* (eds R. M. Post & J. C. Ballenger). Baltimore: Williams & Wilkins.

Pfohl, B., Sherman, B., Schlechte, J., *et al* (1985*a*) Pituitary-adrenal axis rhythm disturbances in psychiatric depression. *Archives of General Psychiatry*, **42**, 897–903.

——, ——, ——, *et al* (1985*b*) Differences in plasma ACTH and cortisol between depressed patients and normal controls. *Biological Psychiatry*, **20**, 1055–1072.

——, Coryell, W., Stangl, D. & Zimmerman, M. (1986) Body weight and reported versus measured weight loss as confounders of the dexamethasone suppression test. *Biological Psychiatry*, **21**, 931–938.

Plotsky, P. (1987) Regulation of hypophysiotropic factors mediating ACTH secretion. In *The Hypothalamic–Pituitary–Adrenal Axis Revisited: a Symposium in Honor of Dorothy Krieger and Edward Herbert. Annals of the New York Academy of Sciences* (eds W. F. Ganong, M. F. Dallman & J. L. Roberts). New York: New York Academy of Sciences.

——, Bruhn, T. & Vale, W. (1985) Hypophysiotropic regulation of adrenocorticotropin secretion in response to insulin-induced hypoglycemia. *Endocrinology*, **117**, 323–329.

Privitera, M. R., Greden, J. F., Gardner, R. W., *et al* (1982) Interference by carbamazepine with the dexamethasone suppression test. *Biological Psychiatry*, **17**, 611–620.

Reisine, T. & Hoffman, A. (1983) Densensitization of corticotropin-releasing factor receptors. *Biochemistry and Biophysics Research Communications*, **3**, 919–925.

Reus, V. I. (1985) Toward an understanding of cortisol dysregulation in major depression: a review of studies of the dexamethasone suppression test and urinary free-cortisol. *Psychiatric Medicine*, **3**, 1–21.

Rivier, J., Spiess, J., Rivier, C., *et al* (1982) Solid phase synthesis of amunine (CRF), sauvagine and urotensin I. In *Proceedings of the 17th European Peptide Symposium, Peptides 1982* (eds K. Blaha & P. Malon). Berlin: Walter de Truyter.

Robins, L., Helzer, J. E., Croughan, J., *et al* (1981) National Institute of Mental Health Diagnostic Interview Schedule. *Archives of General Psychiatry*, **38**, 381–389.

Rosenbaum, A. H., Schatzberg, A. F., MacLaughlin, A., *et al* (1984) The dexamethasone suppression test in normal control subjects: comparison of two assays and effect of age. *American Journal of Psychiatry*, **141**, 1550–1555.

Roy, A., Pickar, D., Paul, S., *et al* (1987) CSF corticotropin-releasing hormone in depressed patients and normal control subjects. *American Journal of Psychiatry*, **144**, 641–645.

Schlesser, M. A., Winokur, G., Sherman, B. M. (1980) Hypothalamic-pituitary-adrenal axis activity in depressive illness. *Archives of General Psychiatry*, **37**, 737–744.

Snedecor, G. W. & Cochran, W. G. (1980) *Statistical Methods* (7th edn). Ames, Iowa: Iowa State University Press.

Spitzer, R. L., Endicott, J. & Robins, E. (1978) Research diagnostic criteria: rationale and reliability. *Archives of General Psychiatry*, **35**, 773–782.

Stokes, P. E., Stoll, P. M., Koslow, S. H., *et al* (1984) Pretreatment DST and hypothalamic–pituitary–adrenocortical function in depressed patients and comparison groups: a multicenter study. *Archives of General Psychiatry*, **41**, 257–267.

Vale, W., Spiess, J., Rivier, C., *et al* (1981) Characterization of a 41 residue ovine hypothalamic peptide that stimulates the secretion of corticotropin and beta endorphin. *Science*, **213**, 1394–1397.

Winer, B. J. (1971) *Statistical Principles in Experimental Design*. New York: McGraw-Hill.

Winokur, G., Pfohl, B. & Sherman, B. (1985) The relationships of historically defined subtypes of depression to ACTH and cortisol levels in depression: preliminary study. *Biological Psychiatry*, **20**, 751–757.

Wynn, P. D., Harwood, J. P., Catt, K. J., *et al* (1985) Regulation of corticotropin-releasing factor (CRF) receptors in the rat pituitary gland: effects of adrenalectomy on CRF receptors and corticotroph responses. *Endocrinology*, **116**, 1653.

Wysham, C., Pfohl, B. & Kathol, R. G. (1986) Arginine vasopressin stimulation and imipramine. *Biological Psychiatry*, **21**, 1351–1355.

Zimmerman, M., Pfohl, B. M. & Coryell, W. H. (1984) Appetite and weight change and the dexamethasone suppression test. *Biological Psychiatry*, **19**, 923–928.

——, Coryell, W. & Pfohl, B. (1986) The validity of the dexamethasone suppression test as a marker for endogenous depression. *Archives of General Psychiatry*, **43**, 347–355.

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Clinical Assessment and Performance Tasks in Depression: a Comparison of Amitriptyline and Trazodone

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Depression, anxiety and psychomotor performance were assessed in 20 depressed patients during double-blind treatment with amitriptyline or trazodone. There was no difference in onset of antidepressant or anxiolytic action. No decrement or improvement on computerised tasks was found. Dry mouth was significantly more frequent and severe with amitriptyline.

The tricyclic antidepressants remain the yardstick against which newer remedies are compared, although they can cause troublesome side-effects, particularly those resulting from cholinergic blockade. Moreover, in overdose and in certain forms of heart disease they are toxic, and cardiac arrhythmias are a special cause for concern. There is a need to develop new drugs which are as effective as the tricyclics but which do not have their drawbacks, and trazodone is a candidate for inclusion in this category.

Trazodone, a triazolopyridine derivative, was first synthesised in 1966; chemically it is 2-[3-[4-(3-chlorophenyl)-1-piperazinyl]propyl]-1, 2, 4-triazolo-[4, 3-a] pyridin-3(2H)-one hydrochloride. Trazodone has an unusual pharmacological profile since it has both agonist and antagonist activity in the cerebral serotonin-mediated pathways, it reduces the sensitivity of central beta-adrenoreceptors, and in animals there are no substantial anticholinergic or cardiotoxic effects characteristic of tricyclic antidepressant drugs (Al-Yassiri *et al*, 1981). Clinical studies are consistent with this last finding (Gershon & Newton, 1980; Van de Merwe *et al*, 1984).

The present study was undertaken to establish if there are important differential effects on intellectual function, on psychomotor function, or in the speed of onset of antidepressant action of amitriptyline (AMT) as compared with trazodone (TZ).

Method

In a double-blind parallel-group comparison of AMT and TZ, patients in whom primary depressive illness was diagnosed were recruited. Inclusion criteria required the presence of depressed mood out of proportion to the environmental situation, and disabling depressive symptoms (e.g. disturbed affect, loss of interest and energy, and pessimistic thought content) in numbers above those found in the normal population. Furthermore, patients included were those who, in the opinion of the prescribing physician, required treatment with antidepressant drugs.

The patients were aged 18–80 years, suffered from a current episode of depressive illness of less than 18 months' duration, and were in satisfactory physical health. Patients were excluded if they were suffering from other psychiatric disorder (organic or functional), if they had received electroconvulsive therapy (ECT) in the previous three months, if their current episode was severe enough to warrant ECT, if they had received adequate doses of antidepressants in the past seven days (according to the manufacturer's recommendations), if they required other psychotropic drugs (other than small doses of benzodiazepines at night only), or if they were pregnant. In the event, six patients (three in each treatment group) received benzodiazepines at night. Informed consent was obtained from patients before they were accepted for the study, and ethical approval was obtained before any patient was started on treatment.

Following one week on placebo (single-blind phase), patients with a score of 17 or more on the 17-item Hamilton Depression Rating Scale (HDRS; Hamilton, 1967) were allocated to three weeks of active treatment according to a predetermined randomisation which was stratified for age (above or below 50) and sex.

After the placebo week, active medication was given as matched capsules of AMT (25 mg) or TZ (50 mg). Between days 8 and 14, the daily doses of AMT and TZ were 75 mg and 150 mg respectively, administered in divided doses twice daily, with the larger portion of the dose taken in the evening. Between days 15 and 21, increased doses of 150 mg and 300 mg respectively were administered. Thereafter, a flexible dosage regimen applied according to the patients' clinical response: the maximum allowable doses for AMT and TZ were 200 mg and 400 mg respectively. Only one patient improved substantially on placebo, and was not entered into the analysis.

On entry to the study, a full clinical assessment was made and the following scales were completed: the HDRS Montgomery–Åsberg Depression Rating Scale (MADRS; Montgomery & Åsberg, 1979), the States of Anxiety and Depression scales (SAD; Bedford *et al*, 1976), the Newcastle Diagnostic Scale (Carney *et al*, 1965), and an overall Severity of Illness scale (1, normal – not at all ill; 2, borderline mentally ill; 3, mildly ill; 4, moderately ill; 5, severely ill; 6, among the most severely ill patients).

On days 8 (first day of active treatment), 12, 15 and 29, the same psychometric assessments were administered, except that the MADRS was omitted on day 12. Also administered was a Global Improvement Scale with respect to the start of active medication (0, not assessed; 1, very much improved; 2, much improved; 3, minimally improved; 4, no change; 5, minimally worse; 6, much worse; 7, very much worse).

A battery of computerised performance tasks of known sensitivity – consisting of simple and choice reaction times, a tracking task and an arithmetic test (McManus *et al*, 1983) – was administered at entry and on days 1, 3, 4, 8 (placebo period), 12, 15, 22 and 29 (double-blind treatment period).

Patients were assessed twice on each test at each visit, except on the first occasion, when each test was administered three times to allow for a learning effect. For the purpose of statistical analysis, the mean score on each day was considered.

Subjective reports on total sleep duration and the perceived quality of sleep were assessed, using the relevant two questions from the St Mary's Hospital Sleep Questionnaire (Ellis *et al*, 1981), on each of the first 15 days of the study (seven days on placebo, eight days on active treatment).

A checklist for pre-existing events was completed before treatment started, with side-effects being monitored on days 8, 12, 15 and 19. Patients were asked both an open-ended question, "Have you had any problems which you think might be due to the tablets?", and subsequently about specific side-effects. For the specific questions, the clinician rated the frequency and severity of nine side-effects (dry mouth, blurring of vision, constipation, nausea, vomiting, headaches, drowsiness, dizziness and tremors) on all occasions except days 1, 3 and 4. The ratings of severity were 'mild', 'moderate', and 'severe', and the ratings of frequency were 'some of the time', 'most of the time', and 'all of the time'.

The statistical analysis was carried out using univariate and multivariate techniques. Analyses of individual variables across a number of testing days were by analysis of variance with both within-subject and between-subject factors, implemented using the MANOVA technique. Analyses of results on particular testing days were by the unpaired *t*-test. Simultaneous analysis of several dependent variables on a number of testing days was by multivariate analysis of variance using the MANOVA technique.

Results

Ten patients were allocated to each treatment group. The groups did not differ significantly in terms of age (AMT – mean 49.2 years, s.d. 23.2; TZ – mean 45.6 years, s.d. 14.4), sex (AMT – 4 male, 6 female; TZ – 3 male, 7 female), in-patient/out-patient status (AMT – 3 in-patients, 7 out-patients; TZ – 4 in-patients, 6 out-patients), type of depression as rated on the Newcastle score (AMT and TZ – 5 reactive and 5 endogenous each), or severity of illness as judged by the 17-item HDRS (AMT – 29.9, s.d. 2.9; TZ – 27.1, s.d. 3.1). Three patients did not complete the study due to side-effects (2 patients on AMT complained of dry mouth and drowsiness; 1 patient on TZ complained of headache): these patients' results were not included in the analysis.

Clinical rating scales

The separate clinical rating scales showed high correlations one with another (range 0.550–0.911), and factor analysis revealed two separate independent dimensions: 'Depression', represented well by the MADRS (loading 0.828), and 'Anxiety', represented by the anxiety scale of the SAD (loading 0.909). Only these scales will therefore be reported here.

Statistical analysis used *a priori* comparisons to assess change during the placebo period, and at days 12–29 relative to the placebo period. Differences between drugs were assessed by examination of the interactions between drug type and these comparisons. The MADRS (Fig. 1(a)) showed no evidence of improvement during the placebo period ($P>0.1$), and then a significant improvement at day 15 ($P<0.001$) and at day 29 ($P<0.001$). Tests for interactions of drug and contrasts showed no significant differences ($P>0.1$) between either of the drugs at any time.

Analysis of the anxiety scale of the SAD (Fig. 1(b)) showed a significant improvement even during the placebo period ($P<0.01$), and then further improvements by day 15 ($P<0.01$) and day 29 ($P<0.001$). Interactions of drug and contrasts showed that the trazodone group was significantly less anxious at day 12 ($P<0.01$), although this difference had disappeared by days 15 and 29.

Performance tests

A priori contrasts were used to assess learning effects during days 1–4, the stability of the baseline during days 4–8, and then change relative to the baseline during days 12–29. Analysis of performance on all of the four tasks showed a similar pattern of results, and only reaction time and addition tasks are shown in Fig. 1(d) and (e). Highly significant learning effects were present during days 1–4 ($P<0.001$) for all tasks (except simple reaction time). In all tasks the baseline was stable over days 4–8, and no tasks showed evidence for significant improvement at days 12–29 relative to baseline. None of the tasks showed any statistically significant evidence for differences between the two drugs, during learning, baseline or drug-treatment phases of the study.

Sleep

Quality and duration of sleep were assessed by *a priori* comparisons of sleep during the placebo and the active period, and linear trends within each of these periods, and their interaction with drug type. Sleep quality (Fig. 1(g)) improved significantly during treatment with the active drug ($P<0.001$), but there were no differences between the two drugs. Sleep duration (Fig. 1(h)) increased on amitriptyline, but not on trazodone, although the effect did not reach statistical significance.

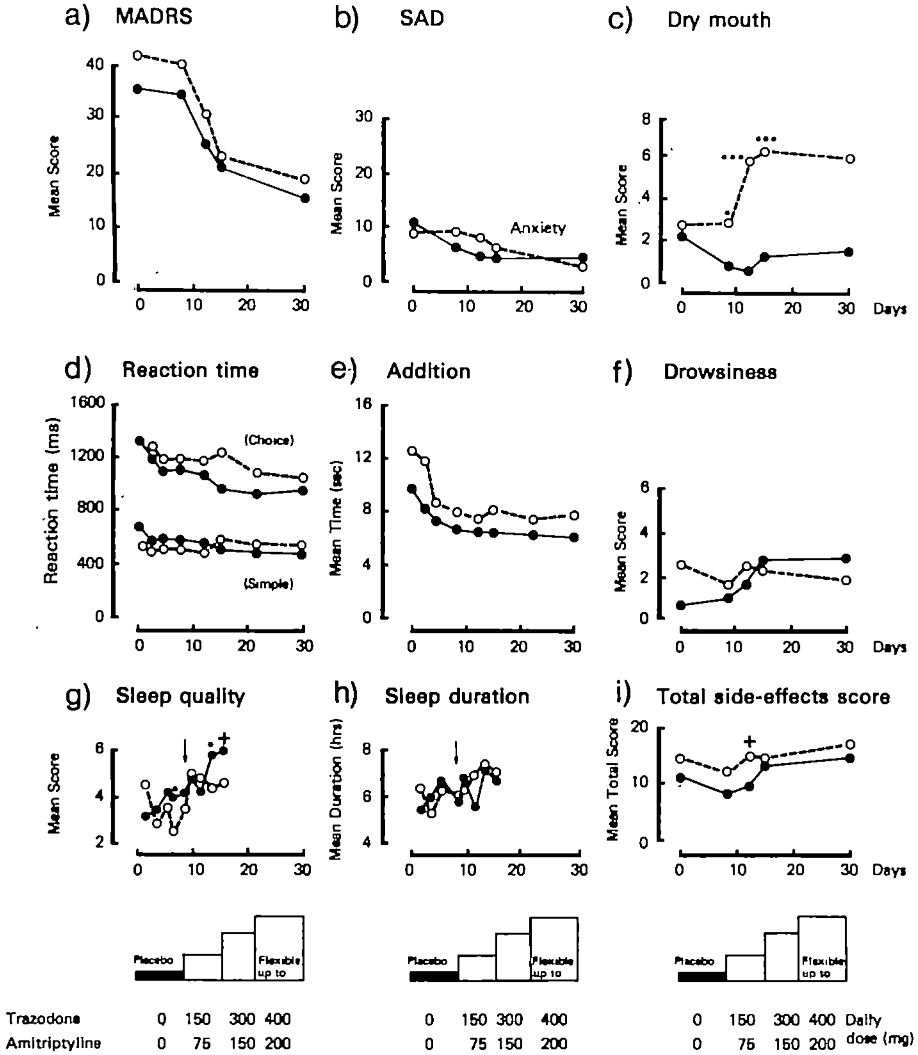

FIG. 1 Results of the assessment of antidepressant (MADRS) and anxiolytic (sAD) activities, performance tests (reaction time and addition tasks), sleep quality and sleep duration, and side-effects (dry mouth, drowsiness and total side-effect score) for patients receiving AMT (○) or TZ (●). $+P<0.1$; $\cdot P<0.05$; $\cdots P<0.001$; ↓ start of active treatment.

Side-effects

Side-effects were assessed by means of a composite score for each side-effect, calculated by multiplying ratings of severity and frequency. The nine side-effects were considered separately, and were also combined in a single overall score. 'Dry mouth' showed a significant increase during active treatment ($P<0.02$) (Fig. 1(c)), but a highly significant interaction with drug treatment ($P<0.005$) showed that this effect was only present in those treated with amitriptyline. Drowsiness (fig. 1(f)) also showed a significant effect of active treatment ($P<0.05$), but there was no significant difference between the drugs ($P>0.1$). Nausea, blurred vision, vomiting, dizziness, constipation, headache, and tremor showed no significant differences either between active and inactive treatments, or between the two drugs. The total side-effects score (Fig. 1(i)) showed a slight tendency to increase during active treatment ($P<0.1$), but there was no significant difference between the two drugs.

Discussion

The patients allocated to AMT and TZ were well matched, and no serious difference in the groups developed as regards dosage change or discontinuation of active treatment. Both drugs had a significant effect in reducing symptoms of depression, but there was no substantial difference between the two treatment groups. However, with a relatively small number of patients, the sensitivity of the measurements may not have been sufficient to provide adequate statistical power to detect differences between the active treatments.

Patients receiving TZ showed an earlier remission of anxiety, which confirms previous reports (Al-Yassiri *et al*, 1983). This is an important subjective improvement in the patient's response and may provide an indication for the use of this drug in the high proportion of depressed patients who also are anxious.

Both drugs improved sleep quality, but a trend for increased duration of sleep was noted with AMT only, a finding similar to that of Montgomery *et al* (1983). Since both drugs cause drowsiness, it is interesting that only AMT caused an increase in duration of sleep, despite the fact that TZ had an early anxiolytic effect (an effect frequently associated with soporific action).

The absence of significant differences on the psychomotor tests is unlikely to be due to an inappropriate bluntness of the tests themselves, since the tests have been shown (McManus *et al*, 1983) to be sensitive to the effects of benzodiazepine and of alcohol. In addition, each of the measures shows clear learning effects within the present study. Nevertheless, even during the period of frank clinical improvement (days 15–29), performance on the psychomotor tasks remained substantially impaired.

The symptoms of blurred vision, constipation, nausea, vomiting, headache, dizziness, and tremor appeared not to be induced by either drug, although drowsiness seemed to be a product of both, and dry mouth an effect of AMT only. Drowsiness is the most frequent side-effect that has been reported for TZ in previous studies (Brogden *et al*, 1981).

In conclusion, the results of the present study fail to suggest an important difference in the onset of antidepressant activity between AMT and TZ. However, the anticholinergic effect of dry mouth was more frequent and severe in the AMT group than in the TZ group.

References

Al-Yassiri, M. M., Ankier, S. I. & Bridges, P. K. (1981) Trazodone – a new antidepressant. *Life Science*, **28**, 2449–2458.

——, —— & —— (1983) A double blind comparison of the efficacy and safety of trazodone and imipramine in endogenous depression. *Journal of Affective Disorders*, **5**, 333–340.

Bedford, A., Foulds, G. A. & Sheffield, B. F. (1976) A new personal disturbance scale (DSSI/SAD). *British Journal of Social and Clinical Psychology*, **15**, 387–394.

Brogden, R. N., Heel, R. C., Speight, T. M., *et al* (1981) Trazodone: a review of its pharmacological properties and therapeutic use in depression and anxiety. *Drugs*, **21**, 401–476.

Carney, M. W. P., Roth, M. & Garside, R. F. (1965) The diagnosis of depressive syndromes and the prediction of ECT response. *British Journal of Psychiatry*, **111**, 659–674.

Ellis, B. W., Johns, M. W., Lancaster, R., *et al* (1981) The St Mary's Hospital sleep questionnaire: a study of reliability. *Sleep*, **4**, 93–97.

Gershon, S. & Newton, R. (1980) Lack of anticholinergic side-effects with a new antidepressant – trazodone. *Journal of Clinical Psychiatry*, **41**, 100–104.

Hamilton, M. (1967) Development of a rating scale for primary depressive illness. *British Journal of Social and Clinical Psychology*, **6**, 278–296.

McManus, I. C., Ankier, S. I., Norfolk, J., *et al* (1983) Effects on psychological performance of the benzodiazepine, loprazolam, alone and with alcohol. *British Journal of Clinical Pharmacology*, **16**, 291–300.

Montgomery, S. A. & Åsberg, M. (1979) A new depression scale designed to be sensitive to change. *British Journal of Psychiatry*, **134**, 382–389.

Montgomery, I., Oswald, I., Morgan, K., *et al* (1983) Trazodone enhances sleep in subjective quality but not in objective duration. *British Journal of Clinical Pharmacology*, **16**, 139–144.

Van de Merwe, T., Silverstone, T., Ankier, S. I., *et al* (1984) A double blind, non-crossover, placebo controlled, between group comparison of trazodone and amitriptyline on cardiovascular function in major depressive disorder. *Psychopathology*, **17**, (Suppl. 2), 64–76.

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Is Diazepam an Antidepressant?

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In double-blind sequential study, diazepam was compared with the proven antidepressant moclobemide, in patients with atypical depression. Both agents significantly improved depression ratings over eight weeks of treatment. Diazepam was a significantly better antidepressant than moclobemide at four weeks, although not at eight weeks. All patients ceased diazepam within one year and none reported withdrawal reactions. These data suggest the need to reconsider that benzodiazepines may be antidepressants and to study their possible antidepressant actions.

Benzodiazepines (BZDs) were not regarded as having antidepressant properties by the Committee on the Review of Medicines (1980). This opinion is supported by research studies, notably the 1980 Medical Research Council study (Johnstone *et al*, 1980) and the Lipman *et al* (1986) and Kahn *et al* (1986) comparisons of imipramine and chlordiazepoxide in depressive and anxiety disorders. The review of studies of benzodiazepines in depressive illness by Johnson (1983) reaffirmed their ineffectiveness in depression, but added that data claiming benzodiazepines can cause depression was anecdotal and without substantial proof.

The condition endogenous, endomorphogenic or major depression with melancholia forms a subtype of depression which is likely to respond to tricyclic antidepressants (TCAs) and electroconvulsive therapy (Klein, 1974; Stern *et al*, 1980). The report of Liebowitz *et al* (1984) showing the superiority of phenelzine over imipramine in atypical depression suggested a subtype of depression responsive to monoamine oxidase inhibitors (MAOIs). It was decided to test the efficacy of the reversible, MAO-A-selective antidepressant moclobemide (p-chloro-N-(2-morpholinoethyl)benzamide, Roche) in atypical depression. Moclobemide has been shown to be an effective antidepressant in both open and double-blind placebo-controlled studies of depressed patients (Stefanis *et al*, 1982; Cassachia *et al*, 1984). It has comparable antidepressant activity to amitriptyline in endogenous and reactive depression (Norman *et al*, 1985), to clomipramine in patients with chronic, episodic, or atypical depression (Larsen *et al*, 1984), and to desipramine in unipolar, bipolar and other depressions (Stefanis *et al*, 1984).

In studying a new antidepressant, it is desirable to compare it with placebo. There are, however, arguments that it is unethical to have patients on inactive preparations for prolonged periods, with the risk of increased morbidity and mortality, when there are effective antidepressants. This problem is commonly resolved by comparing the new antidepressant with an established antidepressant. There may be flaws in such comparisons. The proportion of patients not responding to tricyclics can be 30% (Medical Research Council, 1965) to 40% (Prien *et al*, 1984). Data shows that tricyclic antidepressants were not superior to placebo in 35% (Morris & Beck, 1974) and 41% of studies (Thomson, 1982). Furthermore, inactive placebo is associated with significant improvement in 30% (Morris & Beck, 1974) to 50% (Medical Research Council, 1965) of depressed patients. One must determine comparison doses and dose schedules of antidepressants, and consider that unique side-effects of one medication can confound attempts to achieve blindness in assessments by astute clinicians.

In the assessment of moclobemide in atypical depression it was decided to compare it with diazepam, an agent stated to have no intrinsic antidepressant activity. Diazepam could relieve some anxiety in these patients and as a consequence relieve some distress for the minimum four weeks needed to determine antidepressant efficacy (Baldessarini, 1985), and, it was hoped, for up to eight weeks. Diazepam was regarded as an inactive placebo for antidepressant activity. A closed repeated significance test (RST) sequential design was used (Armitage, 1975), considering antidepressant score alone. This design would stop the trial as soon as one agent proved significantly better than the other or when a no-significant-difference boundary was reached. This design was a compromise allowing for scientific and ethical considerations.

Method

Patients

In-patients and out-patients at the Royal Melbourne Hospital who met the following criteria for atypical depression were considered for the study:

(a) Research Diagnostic Criteria (Spitzer *et al*, 1978) for major, minor, or intermittent depression
(b) maintained mood reactivity while depressed
(c) two or more of the following: increased appetite or weight gain while depressed, oversleeping or spending more time in bed while depressed, severe fatigue creating a sensation of leaden paralysis or extreme heaviness of arms or legs while depressed; and rejection sensitivity as a trait during adulthood (Liebowitz *et al*, 1984).

Patients were aged over 17 years, had been symptomatic for a minimum of one month, were medically stable, and scored over 17 on the 17-item Hamilton Rating Scale for Depression (HRSD; Hamilton, 1960) after at least seven days without drugs. Patients meeting the above criteria were admitted to the study after giving informed consent according to the guidelines of the National Health and Medical Research Council (1983).

Study design

A double-blind sequential trial with paired patients was carried out. Patients were paired according to sex, age (±5 years), and HRSD (±5 points), and allocated to treatment by one of the authors (KM), who was not involved in the clinical assessments. Those patients who were not matched immediately were allocated to treatment on a random basis and matched with the next suitable patient. All patients followed dietary and medication restrictions as for standard irreversible non-selective MAOI antidepressants.

Assessments

Depression was assessed using the observer-rated HRSD and the subject-rated Carroll Depression Rating Scale (CDRS; Carroll *et al*, 1981). Each patient was classed by the Newcastle Scale (Holden, 1983) as endogenously depressed (score 6 or more) or neurotically depressed (score <6). An open-ended side-effects check-list was completed at each assessment. Only emergent side-effects, not present at baseline, were included in the final analysis. Ratings were completed at baseline and after one, four and eight weeks of treatment.

Medication

Following a drug-free week, an initial total daily dose of 15 mg of diazepam or 150 mg of moclobemide was started with equally divided doses three times a day. A double-dummy technique was used, each patient taking active tablets of one medication and inactive placebos made to look like the other medication. The daily dose of medication could be increased, as tolerated, on clinician judgement up to maximum daily doses of 45 mg of diazepam or 450 mg of moclobemide. The 45 mg maximum dose of diazepam was to relieve anxiety in the severely agitated, although it was expected that few would take more than 20–30 mg daily. Nitrazepam (5–10 mg) was permitted as a hypnotic for all patients as required.

Analysis of results

The dimensions of the RST sequential plan were set as $\theta = 0.80$, power 0.95 and overall significance 0.05. Preferences for either drug were based on changes in the HRSD scores, a decrease of 8 points being considered a clinical improvement (Norman *et al*, 1985). Ties were not recorded on the plan, and separate analyses were done at weeks 4 and 8. In addition, the two groups were compared at baseline and weeks 1, 4 and 8 using Student's *t*-tests. The finding of diazepam's antidepressant activity resulted in an analysis, not in the initial design, of specific items of the HRSD to try to preclude anti-anxiety effects being regarded as antidepressant effects.

Results

Sequential analysis

Forty patients with atypical depression entered the study and 31 completed four weeks' treatment. Of these, 28 could be paired for the sequential analysis (including three pairs with age differences of 6, 7 and 10 years). When the week 4 HRSD plan reached a significance boundary, intake for the study ceased as designed, the result showing that diazepam was significantly better (Fig. 1). The results for the 14 pairs included two ties, eleven wins for diazepam and one win for moclobemide. By week 8, the number of tied results had increased from two to seven, and thus the plan did not reach any boundary (Fig. 2).

Comparison of drug groups

For the 14 pairs of patients who completed four weeks' treatment, there were no significant differences at baseline between treatment groups in sex, mean age, HRSD, CDRS,

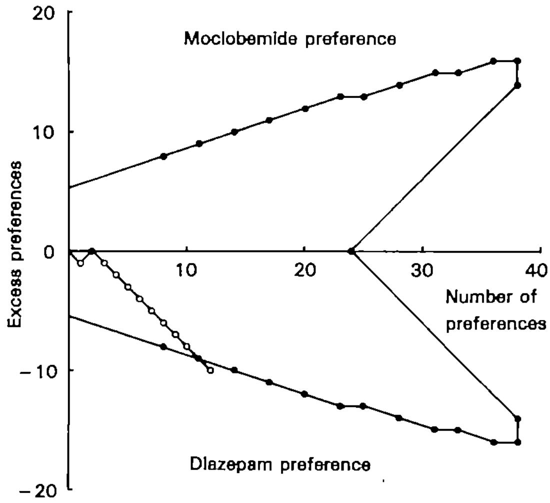

FIG. 1 Sequential analysis of diazepam and moclobemide after four weeks of treatment.

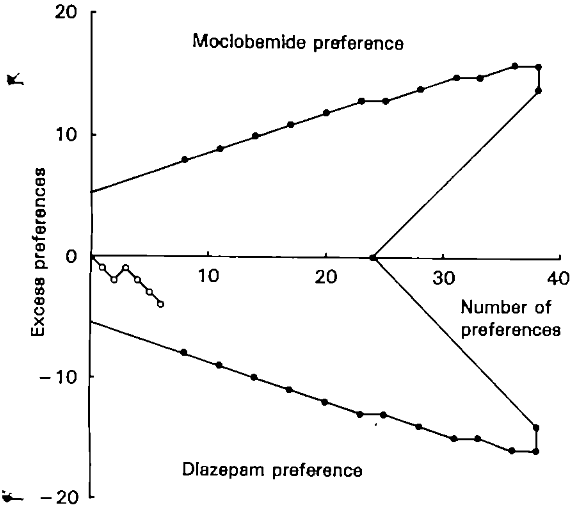

FIG. 2 Sequential analysis of diazepam and moclobemide after eight weeks of treatment.

Newcastle Scale score, or side-effects ratings. There were 14 females and 14 males, with an age range of 21–66 years. All patients met the Newcastle Scale criteria for neurotic depression, the mean score for patients in the diazepam group being 1.0 (s.d. 1.8) and for those in the moclobemide group 1.2 (s.d. 2.0). Results on parameters other than the HRSD and CDRS are reported elsewhere (Tiller *et al*, 1989).

There was a significant decrease in the HRSD and CDRS ratings for the diazepam group from baseline to weeks 1 and 4, and for the moclobemide group from baseline to week 4 (Table I).

The diazepam group had significantly lower HRSD ratings at both weeks 1 and 4 than the moclobemide group, and had a significantly lower CDRS rating at week 1 (Table I).

A separate analysis was made of the ten pairs who completed eight weeks' treatment. Results at weeks 1 and 4 were similar to those obtained for the 14 pairs described above. For both treatment groups, significant decreases in HRSD and CDRS ratings were observed from baseline to week 8 (Table II). At week 8, no significant difference in HRSD scores was found between the two treatment groups, but the CDRS score for the diazepam group was significantly lower than that for the moclobemide group.

TABLE I

HRSD and CDRS scores for the 28 paired patients completing four weeks of treatment

Agent and week		*Diazepam* Mean	s.d.	95% CI	*Moclobemide* Mean	s.d.	95% CI	*t*	P
HRSD	0	22.9	4.5	20.3–25.6	23.1	4.0	20.8–25.5	0.25	0.806
	1	13.1***	6.6	9.4–16.9	23.0	5.1	20.1–25.9	4.45	0.001
	4	9.1***	6.8	5.2–13.1	16.1**	6.3	12.4–19.7	2.82	0.014
CDRS	0	25.8	6.1	22.3–29.3	27.4	5.0	24.5–30.3	0.72	0.487
	1	15.1**	9.7	9.6–20.7	27.9	6.8	24.0–31.3	3.30	0.006
	4	14.4*	12.5	7.2–21.7	21.9*	9.8	16.2–27.5	1.63	0.126

1. CI = confidence interval.
*P<0.05, **P<0.005, ***P<001 for change from baseline (1-tailed).

TABLE II

HRSD and CDRS scores for the 20 paired patients completing eight weeks of treatment

Agent and week		*Diazepam* Mean	s.d.	95% CI	*Moclobemide* Mean	s.d.	95% CI	*t*	P
HRSD	0	22.1	4.7	18.7–25.5	23.0	4.4	19.8–26.2	0.83	0.430
	1	12.0***	5.9	7.8–16.2	23.2	5.9	19.0–27.4	4.83	0.001
	4	6.3***	2.3	4.6–8.0	14.6***	5.9	10.4–18.8	4.64	0.001
	8	6.1***	3.5	3.6–8.6	11.3***	6.1	6.9–15.7	2.17	0.058
CDRS	0	25.4	6.4	20.8–30.0	27.9	5.1	24.2–31.6	1.06	0.316
	1	12.2**	7.0	7.2–17.2	28.0	6.9	23.1–32.9	4.35	0.002
	4	9.1***	7.7	3.6–14.6	21.3**	9.8	14.3–28.3	2.93	0.017
	8	9.0***	7.1	3.9–14.1	18.6**	11.0	10.7–26.5	2.39	0.040

**P<0.005, ***P<0.001 for change from baseline (1-tailed).

TABLE III
HRSD (5 items) for the 20 paired patients completing eight weeks of treatment: the items were depressed mood, guilt, suicidal thoughts, retardation, and loss of libido

	Baseline		*Week 4*		*Week 8*		*Difference from baseline*
	Mean	*s.d.*	*Mean*	*s.d.*	*Mean*	*s.d.*	
Diazepam	4.6	1.7	2.1	1.3	1.6	1.5	$P<0.001$
Moclobemide	6.1	2.0	4.4	2.3	3.0	2.4	$P<0.001$
Difference between groups	NS		$P=0.025$		NS		—

TABLE IV
HRSD item 1 (depressed mood) for the 20 paired patients completing eight weeks of treatment

	Baseline		*Week 4*		*Week 8*		*Difference from baseline*
	Mean	*s.d.*	*Mean*	*s.d.*	*Mean*	*s.d.*	
Diazepam	2.3	0.6	1.1	0.8	0.9	1.0	$P<0.01$
Moclobemide	2.6	0.5	2.1	0.8	1.3	0.9	$P<0.02$
Difference between groups	NS		$P=0.002$		NS		—

Analysis of five HRSD items clinically regarded as most specific to depression and not anxiety also showed significant reductions with diazepam and moclobemide (Table III). These items were depressed mood, guilt, suicidal thoughts, retardation, and loss of libido.

A further analysis was effected considering only the item 'depressed mood' from the HRSD: this also showed significant reductions with diazepam at both weeks 4 and 8 (Table IV).

Dose

Medications were not increased after a clinical response was apparent. Though the maximum allowed diazepam dose was 45 mg, the mean dose used was 32 mg (s.d. 12 mg). For moclobemide the mean dose was 450 mg, as all had reached maximal dose on study criteria before a response was apparent.

Hypnotics

The study patients were not using benzodiazepines at entry to the study apart from two using hypnotics, one temazepam (20 mg at night) and the other nitrazepam (10 mg at night). The numbers of patients using hypnotics at weeks 4 and 8 respectively in the diazepam group were one and none, and in the moclobemide group seven and seven, a significant difference in hypnotic use. Over the whole study, only two of fourteen in the diazepam group used hypnotics, compared with ten of fourteen in the moclobemide group. The maximum hypnotic dose was used in every case. There were no significant differences in depression or anxiety ratings at baseline between those who subsequently used hypnotics and those who did not. At the week 8 assessment of the moclobemide group there were no significant differences in depression or anxiety ratings between the seven on hypnotics and the three on no hypnotics, but the trend was for slightly higher depression and anxiety scores in the group on hypnotics.

Side-effects

Both drugs were well tolerated and side-effects were minimal. The number of reported side-effects decreased during the study for both drugs, as reported in Tiller *et al* (1989). All patients ceased medication within 12 months. Medication was generally ceased by slow reduction, and no patients reported withdrawal reactions with either drug.

Drop-outs

There were no significant differences in age or baseline ratings between the nine drop-outs and the 28 patients completing four weeks treatment. Eight drop-outs completed at least one week of treatment. At week 1 their mean HRSD score (23) was significantly higher than for the 28 completers (18, $P=0.03$). Seven of the eight were on moclobemide, and all but one dropped out before week 4. No drop-out or exclusion was related to adverse medication effects. Seven were due to non-cooperation or non-attendance, one patient had a compensation case which was concealed at entry to the study, and one patient was excluded due to missing data.

Discussion

The results show that diazepam reduced depressive symptoms. This finding was unexpected both in its occurrence and persistence. It was expected that the anxiolytic effects of diazepam would reduce HRSD anxiety items, but not the five selected core depression items nor the item 'depressed mood' alone. These results differ from those of Cassano *et al* (1985), who reported differences between TCAs and BZDs, the former showing significantly greater improvement with depressed mood and the latter with agitation. The authors reported overlap in action for 30% of the subjects in the groups treated with BZDs ($n = 178$) or TCAs ($n = 209$).

The rapid relief of depressive symptoms (within one week) by diazepam was unexpected. Antidepressants can take six weeks to show effectiveness, although improvement may be apparent as early as the first week of treatment (Katz *et al*, 1987). It was expected that any initial benefit of diazepam would be lost with persisting depression (Lipman *et al*, 1986). That was not observed in this study, with HRSD scores falling from baseline to week 8 in both treatment groups.

The rapid effect of diazepam, without the time needed for receptor down-regulation as with other antidepressants, suggests other processes in its mode of action. The elevated levels of the endogenous neuropeptide diazepam-binding inhibitor (DBI) in depression (Barbaccia *et al*, 1986) may represent a functional disinhibition of GABAergic neurotransmission associated with depression. Bartholini *et al* (1986) refer to the direct and indirect evidence for decreased GABAergic function in the pathophysiology of depression, and the efficacy of both direct- and indirect-acting GABAmimetic drugs in treating depression. Diazepam–DBI interactions and their effects on GABAergic transmission may explain why in certain instances benzodiazepines have antidepressant actions, and why the onset of action of diazepam in this study was more rapid and independent of post-synaptic down-regulation.

Hypnotic use was significantly different between the two treatment groups, consistent with the sedative effects of diazepam and the tendency of MAOIs to interfere with sleep. The possibility that apparent antidepressant response, or rapidity of response, in the diazepam group was caused by diazepam blocking benzodiazepine withdrawal symptoms was unlikely, given the limited prior use of benzodiazepines and the fact that the majority of the moclobomide group used a benzodiazepine hypnotic during the study. In the moclobemide group there were no significant differences in response between those taking and those not taking a hypnotic. The trend for slightly higher depression and anxiety scores in the group on hypnotics rendered it unlikely that response in the moclobemide group could be attributed to the hypnotics' actions alone.

Drop-outs were fewer in the diazepam group than the moclobemide group, contrasting with the higher diazepam drop-out rate in the Russell *et al* (1978) comparison with mianserin. Lower early mianserin drop-out may result from mianserin's acute sedative action, which is not present with moclobemide. Most moclobemide drop-out occurred early in treatment, before antidepressant activity was likely to be manifest. Drop-outs were lost to follow-up, with unknown outcomes.

The results showed that both agents were well tolerated, with few side-effects. Sedation was not prominent as an adverse effect with either drug, although patients treated with diazepam had fewer sleep problems and used fewer hypnotics. The gradual increase of drug dosage may account for the lack of sedative side-effects.

Diazepam has been shown previously to be effective in anxious depression (Raskin *et al*, 1974). The Raskin *et al* (1974) study was the only one out of 20 double-blind controlled studies reviewed by Schatzberg & Cole (1978) to show benzodiazepine superiority over an antidepressant in treating depression. Benzodiazepines were equal to antidepressants in nine studies and inferior in ten. Schatzberg & Cole (1978) considered benzodiazepine doses were adequate, but the mean Raskin *et al* (1974) dose (30 mg diazepam) was the highest in their review, and in the present study both maximum and mean doses were higher than in any of their reviewed studies.

Data on the effectiveness of alprazolam as an antidepressant suggests that dose may be of importance. Four such studies (Rickels *et al*, 1982, 1985; Feighner *et al*, 1983; Imlah, 1985) used maximum daily doses of alprazolam of 4.5 mg, 4.5 mg, 4.5 mg, and 3 mg. Considering dose equivalences of 10 mg diazepam to 1 mg of alprazolam (Fabre & McLendon, 1979; Aden & Thein, 1980), the effective doses of alprazolam are similar to those of diazepam in this study. Thus, alprazolam may not have unique antidepressant properties: it is possible that other benzodiazepines, in adequate doses, may be antidepressants.

Diagnosis remains controversial. Anxiety is a common feature of depressive illness (DSM–III) (American Psychiatric Association, 1980), and despite careful study there is still dispute as to whether anxiety and depression are discrete entities (Klerman, 1980) or form overlapping elements in a continuum (Roth *et al*, 1972, Prusoff & Klerman, 1974). This is reflected in different clinicians' concepts of the relationship between anxiety and depression (Goldberg & Simpson, 1985). The use of the term neurosis to describe patients with an admixture of anxiety, depressive and other symptoms has been reconsidered (*British Medical Journal*, 1986).

Akiskal's (1984) paper on the interface of chronic depression with anxiety considered the role of atypical depression and anxious depression as subgroups of depression, while in the general-practice study reported by Goldberg & Simpson (1985) all the patients with depression had anxiety symptoms. It has been suggested that patients with depression and predominant anxiety should be regarded as having an anxiety disorder, not a depression, and be treated with a benzodiazepine (Schatzberg & Cole, 1978). There may need to be a pragmatic decision to divide depressions into those preferentially responsive to tricyclics and other antidepressants, and those responsive to benzodiazepines.

Davis (1985) suggested that the best procedure to test the antianxiety–antidepressant dimension is to determine if benzodiazepines are effective in a group of 'purely depressed patients'. This procedure ignores the possible effectiveness of benzodiazepines in atypical depression. If benzodiazepines in adequate dosage are effective antidepressants in atypical depression, then it would seem inappropriate to use tricyclics, newer antidepressants or MAOIs as the treatments of first choice, when benzodiazepines have greater safety margins, are better tolerated and have less potential toxicity. The rapid onset of benzodiazepine antidepressant activity could minimise patients dropping out of treatment.

There is the possibility of dependency with higher-dose BZDs for the time needed in these patients. This risk of dependency on benzodiazepines and the importance of patient selection has recently been emphasised (Tyrer, 1989). The studies reported by Higgitt *et al* (1985) and Pecknold *et al* (1988) show that gradual reduction of benzo-diazepine dosage avoids or minimises withdrawal reactions, and none occurred in this study.

Improvements observed may not have resulted from medication but represented spontaneous recovery or the non-specific effects of study interventions. Fairchild *et al* (1986) suggested that certain depressions respond to placebo alone. In this study the patients had persistent disorders for at least a month before entry, and remained with a HRSD >17 after at least one week before treatment started, which was thought to minimise the chance of spontaneous recovery.

These results highlight problems in studying drugs. Despite ethical concerns, should one test new drugs and/or new uses by comparisons with an inert agent, rather than an existing treatment, or with a therapeutically active agent presumed ineffective for the condition or symptoms under study?

Benzodiazepines, in adequate doses as shown, may be safe, well-tolerated antidepressants for atypical depression, and more appropriate than conventional antidepressants. This antidepressant activity needs further study, and despite ethical concerns there is a case for a placebo-controlled study. The results also raise the question: are benzodiazepines in adequate doses effective in other types of depression?

References

Aden, G. C. & Thein, S. G. (1980) Alprazolam compared to diazepam and placebo in the treatment of anxiety. *Journal of Clinical Psychiatry*, **41**, 245–248.

Akiskal, H. S. (1984) The interface of chronic depression with personality and anxiety disorders. *Psychopharmacology Bulletin*, **20**, 393–398.

American Psychiatric Association (1980) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn). Washington, DC: APA.

Armitage, P. (1975) *Sequential Medical Trials*. Oxford: Blackwell Scientific Publications.

Baldessarini, R. J. (1985) Drugs and the treatment of psychiatric disorders. In *The Pharmacological Basis of Therapeutics* (eds A. Goodman Gillman, L. S. Goodman, T. W. Rand & F. Murlad). New York: Macmillan.

Barbaccia, M. L., Costa, E., Ferrero, P., *et al* (1986) Diazepam-binding inhibitor. *Archives of General Psychiatry*, **43**, 1143–1147.

Bartholini, G., Lloyd, K. G. & Morselli, P. L. (eds) (1986) *GABA and Mood Disorders, Experimental and Clinical Research, LERS*, vol. 4. New York: Raven Press.

British Medical Journal (1986) Neurosis: another tough old word (Editorial). *British Medical Journal*, **292**, 972–973.

Carroll, B. J., Feinberg, M., Smouse, P. E., *et al* (1981) The Carroll Rating Scale for Depression: development, reliability and validation. *British Journal of Psychiatry*, **138**, 194–200.

Cassachia, M., Carolei, A., Barba, C., *et al* (1984) A placebo-controlled study of the antidepressant activity of moclobemide, a new MAOA-inhibitor. *Pharmacopsychiatry*, **17**, 122–125.

Cassano, G. B., Conti, L., Placidi, G. F., *et al* (1985) The overlap of the spectrum of antianxiety and antidepressant drugs: a multivariate approach. In *Psychiatry – Vol. 1. Clinical Psychopathology: Nomenclature and Classification* (ed. P. Pichot). New York: Plenum Press.

Committee on the Review of Medicines (1980) Systematic review of the benzodiazepines. *British Medical Journal*, **280**, 910–912.

Davis, J. M. (1985) Antidepressant drugs. In *Comprehensive Textbook of Psychiatry IV* (eds H. I. Kaplan & B. J. Sadock). Baltimore: Williams & Wilkins.

Fabre, L. F. & McLendon, D. M. (1979) A double blind study comparing the efficacy and safety of alprazolam with diazepam and placebo in anxious outpatients. *Current Therapeutics Research*, **25**, 519–526.

Fairchild, C. J., Rush, J., Vasavada, N., *et al* (1986) Which depressions respond to placebo? *Psychiatry Research*, **18**, 217–226.

Feighner, J. P., Aden, G. C., Fabre, L. F., *et al* (1983) Comparison of alprazolam, imipramine, and placebo in the treatment of depression. *Journal of the American Medical Association*, **249**, 3057–3064.

Goldberg, D. & Simpson, N. (1985) The diagnosis of anxiety in primary care settings. In *Drug Treatment of Neurotic Disorders: Focus on Alprazolam* (eds M. H. Lader & H. C. Davies). Edinburgh: Churchill Livingston.

Hamilton, M. (1960) A rating scale for depression. *Journal of Neurology, Neurosurgery and Psychiatry*, **23**, 56–62.

Higgitt, A. C., Lader, M. H. & Fonagy, P. (1985) Clinical management of benzodiazepine dependence. *British Medical Journal*, **291**, 688–690.

Holden, N. L. (1983) Depression and the Newcastle scale: their relationship to the dexamethasone suppression test. *British Journal of Psychiatry*, **142**, 505–507.

Imlah, N. W. (1985) An evaluation of alprazolam in the treatment of reactive or neurotic (secondary) depression. *British Journal of Psychiatry*, **146**, 515–519.

Johnson, D. A. W. (1983) Benzodiazepines in depression. In *Benzodiazepines Divided* (ed. M. R. Trimble), pp. 247–259. Chichester: Wiley.

Johnstone, E. C., Cunningham Owens, D. G., Frith, C. D., *et al* (1980) Neurotic illness and its response to anxiolytic and antidepressant treatment. *Psychological Medicine*, **10**, 321–328.

Kahn, R. J., McNair, D. M., Lipman, R. S. *et al* (1986) Imipramine and chlordiazepoxide in depressive and anxiety disorders – II. *Archives of General Psychiatry*, **43**, 79–85.

Katz, M. M., Koslow, S. H., Maas, J. W., *et al* (1987) The timing, specificity and clinical prediction of tricyclic drug effects in depression. *Psychological Medicine*, **17**, 297–309.

Klein, D. F. (1974) Endomorphogenic depression. *Archives of General Psychiatry*, **36**, 447–454.

Klerman, G. L. (1980) Anxiety and depression. In *Handbook of Studies on Anxiety* (eds G. D. Burrows & B. Davies). Amsterdam: Elsevier/North-Holland Biomedical Press.

Larsen, J. K., Holm, P. & Mikkelson, P. L. (1984) Moclobemide and clomipramine in the treatment of depression. *Acta Psychiatrica Scandanavica*, **70**, 254–260.

Liebowitz, M. R., Quitkin, F. M., Stewart, J. W., *et al* (1984) Phenelzine vs. imipramine in atypical depression. *Archives of General Psychiatry*, **41**, 669–677.

Lipman, R. S., Covi, L., Rickels, K., *et al* (1986) Imipramine and chlordiazepoxide in depressive and anxiety disorders – I. *Archives of General Psychiatry*, **43**, 68–77.

Medical Research Council (1965) Clinical trial of the treatment of depressive illness. *British Medical Journal*, *i*, 881–886.

Morris, J. & Beck, A. (1974) The efficacy of antidepressant drugs. *Archives of General Psychiatry*, **30**, 667–674.

National Health and Medical Research Council (1983) *Statement on Human Experimentation and Supplementary Notes*. Canberra: NH&MRC.

Norman, T. R., Ames, D., Burrows, G. D., *et al* (1985) A controlled study of a specific MAO-A reversible inhibitor (Ro 11-1163) and amitriptyline in depressive illness. *Journal of Affective Disorders*, **8**, 29–35.

Pecknold, J. C., Swinson, R. P., Kuch, K., *et al* (1988) Alprazolam in panic disorder and agoraphobia: results from a multicentre trial – III. Discontinuation effects. *Archives of General Psychiatry*, **45**, 429–436.

Prien, R. F. & Levine, J. (1984) Research and methodological issues for evaluating the therapeutic effectiveness of antidepressant drugs. *Psychopharmacology Bulletin*, **20**, 250–257.

Prusoff, B. & Klerman, G. (1974) Differentiating depressed from anxious neurotic outpatients. *Archives of General Psychiatry*, **30**, 302–308.

Raskin, A., Schulterbrandt, J. G., Reatig, N., *et al* (1974) Depression subtypes and response to phenelzine, diazepam, and a placebo. *Archives of General Psychiatry*, **30**, 66–75.

Rickels, K., Cohen, D. O., Csanalosi, I., *et al* (1982) Alprazolam and imipramine in depressed outpatients: a controlled study. *Current Therapeutic Research*, **32**, 157–164.

——, Feighner, J. P. & Smith, W. T. (1985) Alprazolam, amitriptyline, doxepin, and placebo in the treatment of depression. *Archives of General Psychiatry*, **42**, 134–141.

Roth, M., Gurney, C., Garside, R., *et al* (1972) Studies in the classification of affective disorders. The relationship between anxiety states and depressive illness. *British Journal of Psychiatry*, **121**, 147–167.

Russell, G. F. M., Niaz, U., Wakeling, A., *et al* (1978) Comparative double-blind trial of mianserin hydrochloride (Organon GB94) and diazepam in patients with depressive illness. *British Journal of Clinical Pharmacology*, **5**, 57S–65S.

Schatzberg, A. F. & Cole, J. O. (1978) Benzodiazepines in depressive disorders. *Archives of General Psychiatry*, **35**, 1359–1365.

Spitzer, R. L., Endicott, J. & Robins, E. (1978) Research diagnostic criteria: rationale and reliability. *Archives of General Psychiatry*, **35**, 773–782.

Stefanis, C. N., Alevizos, B. & Papadimitriou, G. N. (1982) Antidepressant effect of Ro 11-1163, a new MAO inhibitor. *International Pharmacopsychiatry*, **17**, 43–48.

——, —— & —— (1984) Controlled clinical study of moclobemide (Ro 11-1163), a new MAO inhibitor and desipramine in depressive patients. In *Monoamine Oxidase and Disease: Prospects for Therapy with Reversible Inhibitors* (eds P. Dostert, M. S. Benedetti & K. F. Tipton). London: Academic Press.

Stern, S. L., Rush, A. J. & Mendels, J. (1980) Towards rational pharmacotherapy of depression. *American Journal of Psychiatry*, **137**, 545–552.

Thomson, R. (1982) Side effects and placebo amplification. *British Journal of Psychiatry*, **140**, 64–68.

Tiller, J., Schweitzer, I., Maguire, K., *et al* (1989) A sequential double blind controlled study of moclobemide and diazepam in patients with atypical depression. *Journal of Affective Disorders* (in press).

Tyrer, P. (1989) Risks of dependence on benzodiazepine drugs: the importance of patient selection. *British Medical Journal*, **298**, 102–104.

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Prodromes of Depression and Anxiety
The Stirling County Study

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A longitudinal investigation of psychiatric epidemiology in a general population (the Stirling County study) has indicated that the incidence of depression and anxiety disorders is low relative to prevalence, because these disorders have long durations. In an average year approximately nine adults among 1000 experience a first-ever episode of one of these disorders. Incident cases over the course of a 16-year follow-up were more likely to have had premonitory symptoms than to have been asymptomatic at the beginning of the study. Among the relatively small number of people who exhibited the clearest prodromal manifestations, incidence was 20 per 1000 annually. It might be possible to intervene before such disorders become fully formed and persistent if the precursors are given attention.

In psychiatric epidemiology, studies of prevalence (the proportion of a population ill at one point in time) are much more numerous than studies of incidence (the proportion who become ill for the first time over a defined period of time). While prevalence and incidence are related to each other through the duration of illness, it is generally acknowledged that the two types of studies differ in regard to theoretical and practical importance (Lapouse, 1967; MacMahon & Pugh, 1970).

Based on Morris' (1957) well known outline of the uses of epidemiology, Cooper & Shepherd (1972) suggested that psychiatric epidemiology can provide information for: planning services; understanding the natural history of illness; and studying aetiology. Prevalence investigations are thought to be especially pertinent for practical issues about planning, while incidence studies are thought to be important for aetiological and natural history research.

Building on an earlier study of incidence rates for depression and anxiety disorders in a general population (Murphy *et al*, 1988), the purpose of this study was to investigate the relevance of one type of antecedent in terms of its ability to predict who will become an incident case, and to assess whether subclinical features at a first interview can be considered the prodromes of incident cases of depression and anxiety as determined by a second interview carried out 16 years later.

In focusing on clinical precursors, this report differs from those that have investigated relationships to antecedent social factors, such as life events and adversities (Brown & Harris, 1978; Finlay-Jones & Brown, 1981; Surtees & Rennie, 1983). Thus epidemiology is used to provide information about the natural history of depression and anxiety.

Background Information

The research upon which this report is based is the Stirling County study (Leighton, 1959; Leighton *et al*, 1963; Beiser, 1971; Murphy, 1980). Two types of data have been gathered regarding probability samples of adults residing in the county. One consists of interviews with the sample members themselves, and the other of reports from general practitioners about these same sample members. For the first survey, teams of psychiatrists read the responses to these health interviews, and evaluated the subjects as a basis for estimating the prevalence of psychiatric disorders.

A computer program has now replaced the human evaluation procedure as it pertains to information gathered through structured interviews with subjects (Murphy *et al*, 1985). The program, DPAX, applies principles for case identification and for diagnosis that refer to the essential features of a psychiatric syndrome, to the pattern and frequency of associated symptoms, and to criteria for duration and level of functional impairment.

Where depression is concerned, the first step requires that dysphoric mood be reported in response to a question about the presence and frequency of poor spirits. This is followed by a requirement for positive evidence in *each* of three groups of associated symptoms (disturbances of sleep, appetite, and energy). Following the application of a threshold for the frequency of these symptoms, DPAX requires that the subject responds affirmatively to a question about work impairment owing to poor health, and then to affirm that this has persisted for at least one month. The algorithm for anxiety is similar, but the symptoms involve apprehension, motor tension, and autonomic hyperactivity. The questions in the interview are orientated to the subject's whole life, and the program differentiates between those who are ill at the time of interview and those who had been ill earlier but were recovered at the time of interview.

Most people identified by the program, whether as depressed or anxious, indicate that they are bothered by 'nerves' or feel that they might have a 'nervous breakdown': while this is neither essential nor sufficient for the program to make a diagnosis, it plays the role of an orientating feature and contributes to the category 'residual mixed affective'. This latter category is for persons who are bothered by their 'nerves', but whose specific symptoms are scattered across the domains of depression and anxiety yet do not fulfil the complete criteria for either syndrome. 'Residual mixed affective' is thus different in meaning from a mixture of manic and depressive symptoms.

DPAX not only identifies cases but also divides the non-cases into categories reflecting the degree to which they fail to meet the criteria for being a case, calling them 'borderline', 'conceivable', or 'well'. In using these subthreshold categories, our methods are similar to those developed by other psychiatric epidemiological researchers (Essen-Möller, 1956; Brown & Harris, 1978; Wing *et al*, 1978). The four steps that distinguish 'well', 'conceivable', 'borderline', and 'cases' (case identification) are carried out before the routines by which the diagnoses of 'depression', 'anxiety', and 'residual mixed affective' are given.

The case-identification aspects of the program correspond well to the original evaluations carried out by psychiatrists. Sensitivity ranges from 99% to 92% over the four steps, while specificity improves from 64% to 98% (Murphy *et al*, 1987*a*). With DPAX we have been able to reanalyse the data that were described in the early publications of the Stirling County study, and then to begin to report for the first time the results of repeated cross-sectional surveys and cohort follow-up studies.

The first survey was carried out in 1952, when 1003 adults from a probability sample of 1098 were interviewed, giving a completion rate of 91%. The application of DPAX indicated that the overall point prevalence of depression, anxiety, and 'residual mixed affective' disorders was 12.5% (Murphy *et al*, 1984) (see Table II). We also used DPAX to analyse information from a new sample, selected in 1970, and found that prevalence at that time was similar (12.7%).

TABLE I
Results of follow-up, 1968

Baseline categories[1]	*Decedents*	*Survivors not re-interviewed*	*Survivors re-interviewed*	*Total*
Cases before 1952	4	6	30	40
Cases in 1952	41	15	64	120
Never cases by 1952	197	122	524	843
Total sample	242	143	618	1003

1. Cases are those subjects whose 1952 interview responses met the criteria for having a depression, anxiety, or 'residual mixed affective' disorder as defined by the DPAX computer program.

The relationship between prevalence and sex was also similar in both samples, and in each overall prevalence was higher among older than younger subjects.

In 1968 a follow-up was begun of the people interviewed in 1952. A quarter of the sample had died (Table I); 618 (81%) of the 761 survivors were reinterviewed. Those who were cases in 1952 experienced 1.5 times the expected number of deaths (Murphy *et al*, 1987*b*). Depression, especially among men, was significantly associated with excess mortality, while anxiety was not. Among the 64 cases who survived and were reinterviewed, 26% became long-term chronic cases, with an additional 30% having a poor clinical outcome as evidenced in at least one recurrence, with depression again having significantly worse prognosis than anxiety (Murphy *et al*, 1986).

Where the criteria of both depression and anxiety were completely fulfilled, the analyses of mortality and poor clinical outcome indicated that it was depression that carried the risk. In view of this, a hierarchy is used here, in which depression takes precedence over anxiety. Thus 'depression' should be understood as depression with or without anxiety while 'anxiety' means only anxiety.

For the study of incidence, we focused on the 524 reinterviewed survivors shown in Table I who, according to the DPAX analysis of their 1952 interviews, had never before had a depression, anxiety, or 'residual mixed affective' disorder (Murphy *et al*, 1988). Seventy-two incident cases were identified by the application of the DPAX program to the 1968 interviews. The onset dates were scattered throughout the 16-year period, and the durations of illness were variable above the minimum requirement of one month.

Since we used the same computer program to process information gathered by means of the same interview protocol, the criteria for counting a person as an incident case are identical with those for counting a subject as a prevalent case. When the disorders were grouped together, we found that incidence was 9.2 cases per 1000 adults per year (Table II). As with prevalence, incidence was considerably higher among women than men, owing mainly to anxiety and 'residual mixed affective' disorders. Incidence was also higher among younger persons in contrast to the higher prevalence we found among older people.

The annual incidence of these disorders was low relative to their prevalence (approximately 9 per 1000 compared to 125 per 1000). Such a relationship is typical in the epidemiology of a chronic disorder. Depression and anxiety often ran a chronic or recurrent course. Nevertheless, it is impossible to calculate precisely the average duration of illness from a study that deals with only a portion of the lives of its subjects. Average duration can, however, be estimated by the formula which states that prevalence is the product of incidence and average duration (MacMahon & Pugh, 1970). By this method, the average duration of the disorders identified by DPAX is a little over ten years.

Method

For analysis of the prodromes of incidence, we use as predictor variables the subthreshold categories derived from

Table II

Point prevalence and average annual incidence of depression and anxiety disorders[1]

Subjects	*Depression*	*Anxiety*	*'Residual'*	*Total*
Point prevalence: rates per 100 subjects, 1952				
Men ($n=456$)	4.7 (24)	2.3 (12)	1.2 (4)	8.2 (40)
Women ($n=547$)	6.0 (36)	7.6 (31)	3.1 (13)	16.7 (80)
Total ($n=1003$)	5.3 (60)	5.0 (43)	2.2 (17)	12.5 (120)
Average annual incidence: rates per 1000 subjects, 1952–68				
Men ($n=251$)	2.1 (8)	2.3 (9)	0.3 (1)	4.9 (18)
Women ($n=273$)	2.5 (10)	6.3 (25)	4.8 (19)	13.3 (54)
Total ($n=524$)	2.3 (18)	4.3 (34)	2.5 (20)	9.2 (72)

[1] The disorders were identified by using the DPAX computer program to analyse responses given in interviews carried out for prevalence in 1952 and for incidence in 1968 among subjects who, in 1952, gave evidence that they had never had a DPAX disorder up to that time. When all criteria have been met for depression, this diagnosis takes precedence over similarly complete anxiety. 'Residual' refers to a 'mixed affective' diagnosis in which symptoms are scattered across both syndromes but do not meet the full criteria of either. The rates have been standardised for prevalence by age and districts where different sampling rates were used and for incidence by age. The number of subjects is shown in parentheses.

Table III

Baseline subthreshold categories and subsequent annual incidence of depression and anxiety disorders: rates per 1000 subjects[1]

Subthreshold categories	*Depression*	*Anxiety*	*'Residual'*	*Total*
'Borderline' category ($n=89$)	4.9 (6)	12.2 (15)	3.2 (4)	20.1 (25)
'Conceivable' category ($n=97$)	2.8 (4)	6.4 (9)	2.8 (4)	12.1 (17)
'Well' category ($n=338$)	1.5 (8)	1.9 (10)	2.3 (12)	5.8 (30)
Total ($n=524$)	2.3 (18)	4.3 (34)	2.5 (20)	9.2 (72)

[1] The disorders were identified by using the DPAX computer program to analyse responses given in interviews carried out in 1968. The subthreshold categories were identified by applying the program to interview responses given in 1952. 'Residual' refers to a 'mixed affective' diagnosis in which symptoms are scattered across both syndromes but do not meet the full criteria of either. The rates have been standardised for age and sex, and the number of subjects is shown in parentheses.

the application of DPAX to the interviews conducted in 1952. The 'borderline' category is the most clearly prodromal, in that subjects classified in it reported symptoms that fitted a syndromal pattern, but failed to meet the full criteria for 'caseness' by lacking one or more of the other requisites for symptom frequency, impairment, or duration. The 'conceivable' category is also prodromal, in that subjects reported associated symptoms but lacked the necessary evidence about essential features. The 'well' category refers to a sufficient absence of symptoms of depression and anxiety such that it seems appropriate to say that it does not contain any evidence of clinical prodromes. The outcome variable is incidence, and we assessed the influence of baseline position in reference to sex and to age (divided into three categories for age at the onset of disorder: under 40 years, 40–49 years, and 50 years and over).

A life-table computer program (Monson, 1974) was used to calculate average annual incidence rates for the subthreshold categories. The new disorders reported as having occurred after 1952 were the numerators, and the person-years of observation relevant to the 524 subjects were the denominators. The statistical significance of the effects of the predictor variables was assessed using survival regressions as described by Laird & Olivier (1981). The models of analysis employed for the survival regressions assessed the main effect of each subthreshold category when the effects of age and sex were controlled. Interactive effects were also investigated, to see whether the effect of being 'borderline', for example, interacted significantly with the effects of age or of sex.

Results

About two-thirds (338) of the subjects in our study population who were at risk for a first disorder presented themselves as being 'well' in 1952. The remainder reported some positive evidence, with 97 subjects being in the 'conceivable' category at that time, and 89 in the 'borderline' category. As shown in Table III, these subthreshold categories bore a highly significant and clearly gradient relationship to subsequent incidence of the combined disorders ($P<0.001$).

The highest risk was associated with the 'borderline' category, the lowest related to the 'well' category. This order pertained in all diagnostic categories, but was significant only for anxiety ($P<0.001$). This information suggests

TABLE IV

Subthreshold categories at baseline and at follow-up among subjects who were never cases[1]

Subthreshold categories 1952	*Subthreshold categories in 1968*		
	'Borderline' (n=*44)*	*'Conceivable'* (n=*119)*	*'Well'* (n=*289)*
'Borderline' ($n=64$)	25%	27%	48%
'Conceivable' ($n=80$)	11%	36%	53%
'Well' ($n=308$)	6%	24%	70%

1. The subjects in this table are 452 persons whose interview data indicated that they were never cases during the study (i.e. 524 non-cases according to the 1952 information minus the 72 incident cases based on the 1968 interviews). The number of subjects is shown in parentheses and the percentages refer to the baseline positions that are shown in the rows.

TABLE V

Baseline categories and subsequent outcome among surviving reinterviewed subjects

Baseline categories in 1952[1]	*Ill at some point after 1952*[2]
Ill at time of 1952 interview ($n=64$)	56%
Ill earlier but recovered by time of interview ($n=30$)	40%
'Borderline' category ($n=89$)	28%
'Conceivable' category ($n=97$)	18%
'Well' category ($n=338$)	9%
Total ($n=618$)	19%

1. The baseline categories were derived from the application of the DPAX program to the 1952 interviews. The information contained in the baseline categories indicates that current prevalence in 1952 was 10.4% (64 divided by 618). This differs from the 12.5% reported for the parent sample of 1003 subjects because the subjects in this table survived and did not therefore reflect the increased mortality risk we found to be associated with depression (Murphy *et al*, 1984, 1987*b*).
2. Proportions of subjects in the baseline categories who were chronic, recurrent, or incident cases as derived from the application of the DPAX program to the 1968 interviews.

that the onset of these disorders tends to be insidious. Several of the subjects who developed these incident disorders in adulthood said that they had been bothered by nervousness or other central symptoms since childhood or adolescence. However, there were no significant interactions between the baseline positions and age, and only one possibly significant interaction ($P=0.049$) with sex (men who became depressed were somewhat more likely than women to have been 'well' earlier).

In Table IV relationships between the subthreshold categories at baseline and follow-up are shown for subjects who never became cases throughout the study.

The percentages for those ill during the study period are strongly and regularly related to the baseline categorisation (Table V). Outcome was worse among those who were ill at the time of the first interview and best among those who were well at that time.

The depression and anxiety symptom inventory of the interview protocol used for the DPAX program (the Health Opinion Survey; Macmillan, 1957) was scored by counting the symptoms endorsed and weighting them for their frequency of occurrence. The product–moment correlation between the 1952 scores and the 1968 scores is 0.57. This relatively high test–retest correlation is in keeping with the stability of the profile shown in Table V.

Discussion

Incidence of depression and anxiety disorders is low relative to prevalence, because of chronicity. The incidence rates may err on the side of being somewhat lower than true incidence because the subjects who died (and who were therefore not reinterviewed) may have had higher incidence than the survivors upon whom our estimates are based (Murphy *et al*, 1988). It is also possible that some disorders of short duration were not recalled, or that recall was influenced by the current clinical state, as has been suggested in other studies (Bromet *et al*, 1986).

However, it seems that the rate of about nine per 1000 per year is more realistic than the higher rates reported from some one-year follow-up investigations. A study of women in Edinburgh, for example, suggests that the incidence of depression and anxiety over one year is 126 per 1000 (Surtees *et al*, 1986). If the year of this study was typical, by the end of ten years nearly three-fourths of the women would have become incident cases. It seems unlikely that depression and anxiety afflict such a large portion of the population *de novo* over such a short period. Perhaps some of the women, while being well at the beginning of the study, were actually in a phase of remission, and that the incidence rate refers mainly to attacks of depression and anxiety that were recurrences rather than first-ever episodes.

A main finding in this paper is that the onset of anxiety, and to a lesser extent of depression, appears to be a clinical process of considerable time depth, sometimes dating back to youth. For example, the risk for subsequent disorder associated with the 'borderline' category as determined by evidence given 16 years earlier was over three times that associated with the 'well' category. Among those who did not become incident cases, sizeable portions of those classified in the 'borderline' or 'conceivable' categories at baseline stayed in these same categories according to the follow-up evidence. The latter suggests that some subjects remained in a subclinical state, continuing to be at risk for a full-scale disorder beyond the time span of this study.

Those subjects who became ill tended to emerge from the grey area between illness and health. Yet, on the whole, during the 1950s and 1960s a minority of the population of Stirling County was ill, and this proportion tended to stay ill, while a majority was well and tended to stay well. These findings and the 1952–68 test–retest correlation emphasise the stability of the illness/health distribution over time.

If this study is correct in suggesting that depression and anxiety tend to be chronic or recurrent disorders with low incidence relative to prevalence in adulthood, serious problems are posed for prevention. Without clues about who is likely to become ill, a preventive intervention would need to be so safe and so inexpensive that it could be applied to the full thousand as a means of reaching those nine who will become ill in any given year. Since the mental health field lacks such preventive methods, there is correspondingly greater need to learn how to pose barriers to a person's moving from 'borderline', for example, to the full status of being a case.

The evidence reported here was gathered by asking direct and simple questions. The fact that the data came from an inquiry about health suggests that general practitioners (GPs) might be particularly well placed to detect people who have such forerunning symptoms and to help prevent them from developing a full disorder.

A number of GP studies have found that physicians are often unaware of the emotional problems of their patients, constituting what has come to be called 'hidden psychiatric morbidity' (Kessel, 1960; Shepherd *et al*, 1966). The reasons that GPs fail to recognise depression and anxiety are not clearly understood, but it is possible that they do not ask about depressed and anxious moods and, if they do inquire, may neglect to pursue the topic systematically in understandable language. If GPs are to play a role in prevention, it will be important to increase for them the visibility of premonitory features, and for this purpose questions such as those employed by the DPAX program and those in a number of screening instruments might be helpful (Goldberg, 1972; Derogatis *et al*, 1974; Radloff, 1977).

Cases identified in community surveys have sometimes been thought of as suffering 'minor psychiatric morbidity' in contrast to the major disorders treated in hospitals and out-patient services (Burvill & Knuiman, 1983). Cases in the community have been interpreted as reflecting transient mood disturbances that are more in keeping with the concept of 'demoralisation' than with 'true illness' (Duncan-Jones & Henderson, 1978; Link & Dohrenwend, 1980). Our findings do not support such a conclusion. Depression and anxiety disorders appear on the whole to be neither short in duration nor minor in regard to distress and disability. In another study carried out in Stirling County, a subsample of 123 people divided about equally between psychiatrically ill and well subjects was interviewed annually for five years by psychiatrists (Beiser, 1971). Clinical observation of these community residents also emphasised low rates of new cases, and high rates of chronicity. If we add to this the evidence that depression was associated with excess mortality risk, findings from the Stirling County study suggest that the search for preventive interventions is made compelling by the fact that these disorders, when they do occur, reduce both the quantity and quality of life.

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References

Beiser, M. (1971) A psychiatric study of 'normal' adults. *American Journal of Psychiatry*, **127**, 1464–1472.

Bromet, E. J., Dunn, L. O., Connell, M. M., *et al* (1986) Long-term reliability of diagnosing lifetime major depression in a community sample. *Archives of General Psychiatry*, **43**, 435–440.

Brown, G. W. & Harris, T. (1978) *Social Origins of Depression: A Study of Psychiatric Disorder in Women*. New York: The Free Press.

Burvill, P. W. & Knuiman, M. W. (1983) Minor psychiatric morbidity and general practice consulting rates. *Psychological Medicine*, **13**, 635–643.

Cooper, B. & Shepherd, M. (1972) Epidemiology and abnormal psychology. In *Handbook of Abnormal Psychology* (2nd edn) (ed. H. J. Eysenck). London: Pitman.

Derogatis, L. R., Lipman, R. S., Rickels, K., *et al* (1974) The Hopkins Symptom Checklist (HSCL): a self-report symptom inventory. *Behavioral Sciences*, **19**, 1–15.

Duncan-Jones, P. & Henderson, S. (1978) The use of a two-phase design in a prevalence survey. *Social Psychiatry*, **13**, 231–237.

Essen-Möller, E. (1956) Individual traits and morbidity in a Swedish rural population. *Acta Psychiatrica et Neurologica Scandinavica* (suppl. 100), 1–160.

Finlay-Jones, R. & Brown, G. W. (1981) Types of stressful life events and the onset of anxiety and depressive disorders. *Psychological Medicine*, **11**, 803–815.

Goldberg, D. P. (1972) *The Detection of Psychiatric Illness by Questionnaire*. London: Oxford University Press.

Kessel, W. I. N. (1960) Psychiatric morbidity in a London general practice. *British Journal of Preventive and Social Medicine*, **14**, 16–20.

LAIRD, N. & OLIVIER, D. C. (1981) Covariance analysis of censored survival data using log-linear analysis techniques. *Journal of the American Statistical Association*, 76, 231–240.

LAPOUSE, R. (1967) Problems in studying the prevalence of psychiatric disorder. *American Journal of Public Health*, 57, 947–954.

LEIGHTON, A. H. (1959) *My Name is Legion: The Stirling County Study of Psychiatric Disorder and Social Environment*. New York: Basic Books.

LEIGHTON, D. C., HARDING, J. S., MACKLIN, D. B. *et al* (1963) Psychiatric findings of the Stirling County study. *American Journal of Psychiatry*, 119, 1021–1026.

LINK, B. & DOHRENWEND, B. P. (1980) Formulation of hypotheses about the true prevalence of demoralization in the United States. In *Mental Illness in the United States: Epidemiological Estimates* (ed. B. P. Dohrenwend, *et al*), pp. 114–132. New York: Praeger.

MACMAHON, B. & PUGH, T. F. (1970) *Epidemiology: Principles and Methods*. Boston: Little Brown.

MACMILLAN, A. M. (1957) The Health Opinion Survey: technique for estimating prevalence of psychoneurotic and related types of disorder in communities. *Psychological Reports*, 3, 325–339.

MONSON, R. R. (1974) Analysis of relative survival and proportional mortality. *Computers and Biomedical Research*, 7, 325–332.

MORRIS, J. N. (1957) *Uses of Epidemiology*. London: E. & S. Livingstone.

MURPHY, J. M. (1980) Continuities in community-based psychiatric epidemiology. *Archives of General Psychiatry*, 37, 1215–1223.

——, SOBOL, A. M., NEFF, R. K., *et al* (1984) Stability of prevalence: depression and anxiety disorders. *Archives of General Psychiatry*, 41, 990–997.

——, NEFF, R. K., SOBOL, A. M., *et al* (1985) Computer diagnosis of depression and anxiety: the Stirling County study. *Psychological Medicine*, 15, 99–112.

——, OLIVIER, D. C., SOBOL, A. M., *et al* (1986) Diagnosis and outcome: depression and anxiety in a general population. *Psychological Medicine*, 16, 117–126.

——, BERWICK, D. M., WEINSTEIN, M. C., *et al* (1987*a*) Performance of screening and diagnostic tests: application of receiver operating characteristic (ROC) analysis. *Archives of General Psychiatry*, 44, 550–555.

——, MONSON, R. R., OLIVIER, D. C., *et al* (1987*b*) Affective disorders and mortality: a general population study. *Archives of General Psychiatry*, 44, 473–480.

——, OLIVIER, D. C., MONSON, R. R., *et al* (1988) Incidence of depression and anxiety: the Stirling County study. *American Journal of Public Health*, 78, 534–540.

RADLOFF, L. S. (1977) The CES-D scale: a self-report depression scale for research in the general population. *Applied Psychological Measurement*, 1, 385–401.

SHEPHERD, M., COOPER, B., BROWN, A. C., *et al* (1966) *Psychiatric Illness in General Practice*. London: Oxford University Press.

SURTEES, P. G. & RENNIE, D. (1983) Adversity and the onset of psychiatric disorder in women. *Social Psychiatry*, 18, 37–44.

——, SASHIDHARAN, S. P. & DEAN, C. (1986) Affective disorder amongst women in the general population: a longitudinal study. *British Journal of Psychiatry*, 148, 176–186.

WING, J. K., MANN, S. A., LEFF, J. P., *et al* (1978) The concept of a "case" in psychiatric population surveys. *Psychological Medicine*, 8, 203–217.

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Efficacy of Lithium Prophylaxis in Clinical Practice

H. R. MARKAR and A. J. MANDER

The efficacy of lithium prophylaxis in bipolar affective disorder in clinical practice was investigated. Comparison was made between 41 patients who were prescribed prophylactic lithium after two admissions in two years or three admissions in five years and a group of patients who did not receive lithium. The benefits conferred by the prescription of this drug were modest compared with the results from clinical trials.

Although lithium was first used in the management of acute mania (Cade, 1949), it is no longer the drug of first choice in this condition (Tyrer, 1985). Currently the primary indication for lithium is in the prophylaxis of bipolar disorder, and its value in this condition has been demonstrated in several well designed, placebo-controlled studies (Baastrup *et al*, 1970; Coppen *et al*, 1971; Hullin *et al*, 1972; Prien *et al*, 1973).

Most of these studies have used either the 'discontinuation' design (Baastrup *et al*, 1970; Prien *et al*, 1973), where the possibility of a lithium withdrawal syndrome cannot be excluded, or the 'before and after' design (Hullin *et al*, 1972), in which the natural course of the illness can be a significant factor affecting the results. Few studies have used the 'start' design, in which patients are randomly allocated to lithium or placebo for a given period of time (Coppen *et al*, 1971).

The interpretation of these studies is complicated by differences in diagnostic criteria, length of study, and methods used to evaluate prophylaxis, but there is still overwhelming evidence of lithium efficacy. Prospective clinical trials are closely supervised, ideal situations where compliance is usually 100%, and therefore may not reflect accurately the situation in normal clinical practice.

Symonds & Williams (1981) showed that the readmission rate for mania in the UK had risen despite increased lithium prescription. Similar results have been reported by Baldessarini (1970), Dickson & Kendell (1986), Grof (1987) and Parker *et al* (1985). Further evidence of a difference between clinical practice and prospective trials was provided by Mander (1986), who showed that there was no significant difference in the risk of readmission within two years for those patients who received lithium and for those who did not after the first manic episode.

These data suggest that more studies are needed on lithium prophylaxis and long-term outcome in ordinary clinical situations. The studies need to be retrospective if they are to reflect ordinary clinical practice, for the reasons already discussed.

There are no clear guidelines on when lithium prophylaxis should be started, although it is sometimes recommended that patients should receive prophylactic lithium if they have had two episodes of illness in two years or three episodes within a period of five years. We have therefore used these guidelines in this retrospective study, to assess the efficacy of lithium prophylaxis in an 'intention to treat' group.

Method

Edinburgh is well placed for a retrospective study. All admissions and discharges since 1970 have been recorded in the Edinburgh Psychiatric Case Register (EPCR): the case notes are typewritten; after discharge a comprehensive summary is prepared; and a lithium register is maintained which records details about lithium-treated patients, monitors their serum lithium levels, and sends reminders to doctors when serum lithium estimations and annual checks of thyroid and renal function are due.

All patients who had at least one admission to the Royal Edinburgh Hospital during 1 January 1970 to 31 March 1987 with an ICD-9 diagnosis of manic–depressive psychoses – manic type, or manic-depressive psychoses (mixed) – currently manic (World Health Organization, 1978) were identified by the EPCR. A consecutive series of patients who were first registered with our service before July 1975 were selected from this group for further study. We were unable to trace 65 (12%) sets of records, and a further 71 patients who were deceased by the time of the study were also excluded. Of the remaining 410 case records, 277 had a history of two admissions in 2 years or three admissions in 5 years. These were selected for further study and the following inclusion criteria applied:

(a) DSM-III (American Psychiatric Association, 1980) diagnosis for bipolar affective disorder with at least one admission for mania

(b) The patient was not taking any other prophylactic medication at the time of the index episode (i.e. the second or third admission used for selection of the case)

(c) Only those patients who took lithium continuously for at least six months following the index episode and had a mean serum lithium level > 0.4 mmol/l during this period were included in the lithium group.

The final study group consisted of 83 patients, 41 of whom received lithium prophylaxis and 42 patients who did not – the latter comprised the control group. The majority of the patients in the control group did not receive lithium because their index episode occurred before lithium came into widespread use in Edinburgh, or else they did not take it continuously for six months. A few patients did not receive lithium for other reasons, such as renal impairment, intolerable side effects and unwillingness to go on long-term prophylaxis.

Relapse was defined as readmission to hospital with a clinical diagnosis of mania or depression. Although patients entered the study at different times, they were all brought to a common starting point – the point when they had been well for six months following the index episode. Relapses occurring within six months were considered to be a continuation of the original episode. The data were analysed to 31 March 1987 as follows:

(a) The Actuarial Life Table, Fleiss *et al* (1976) was used. All patients were followed up starting six months post index until the occurrence of a readmission or the end of the study period, whichever was the sooner

(b) The total number of admissions per year in the two groups and the total time spent as an in-patient per year of follow-up were analysed. For this procedure we used the combined mean test, where the number of observations above and below the combined mean in each group were taken, and the χ^2 test (corrected for continuity) was applied (Siegel, 1956).

Results

Demographic and clinical variables are summarised in Table I. Mean age was the only statistically significant difference between the two groups. The difference was still apparent when patients from the control group who had their index episode before 1970 (i.e. before lithium was in general use in Edinburgh) were excluded. It probably indicates a reluctance by the clinicians to initiate maintenance lithium therapy in older patients, but this is

TABLE I
Demographic and clinical variables

Characteristic		*Lithium group* n=*41*	*Control group* n=*42*	*Significance*
Mean age at index episode		41.9	51.8	t=3.83 $P<0.001$
Male/female		17/24	11/31	$\chi^2=1.53$ (NS)
Social class	1	7	3	
	2	7	11	
	3	18	17	K-S[5] Z=0.48
	4	5	5	NS
	5	4	6	
Living group[1] at index episode	0	1	0	
	1	29	35	K-S[5] Z=0.62
	2	1	2	NS
	3	10	5	
Work status[2] at index episode	0	2	0	
	1	2	8	K-S[5] Z=0.50
	2	25	16	NS
	3	1	4	
	4	11	14	
Marital status[3] at index episode	1	10	7	K-S[5] Z=0.41
	2	25	27	NS
	3	6	8	
Mean duration of index episode: weeks		6.09	7.87	K-S[5] Z=0.73 NS
Index episode no.	2/2	32	35	K-S[5] Z=0.19
	3/5	9	7	NS

1. Living group: 0, not known; 1, relative/spouse; 2, lodgings; 3, alone.
2. Work status: 0, not known; 1, unemployed; 2, employed; 3, retired; 4, other/housewife.
3. Marital status: 1, never married; 2, married; 3, separated/widowed.
4. $n=40$ because of insufficient data.
5. Kolmogorov–Smirnov 2-sample test.

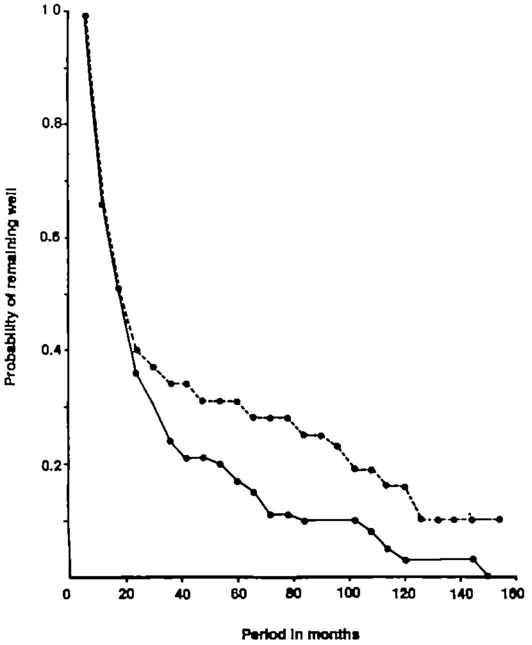

FIG. 1 Probability of remaining well for lithium (●—●) and control (●—●) groups, plotted against time.

the group that is most at risk (Angst *et al*, 1969; Grof *et al*, 1970).

The life tables for the lithium and control groups are represented in Fig. 1, which shows the cumulative probability of remaining well plotted against time. In both groups the failure rate is high and almost equal during the first two years of follow-up. Thereafter the curves diverge, the maximum difference occurring at 72 months.

The summary χ^2 for the entire follow-up period was not significant ($\chi^2 = 1.68$, d.f. $= 1$), and there was no statistical difference at 72 months ($z = 1.83$). Finally, there was no statistical difference in the total number of admissions or the total time spent as an in-patient per year of follow-up (Table II).

Discussion

The dates of the study covered the period during which lithium was introduced to our centre in order to ensure that we would have sufficient numbers in the control group. We used the EPCR to identify cases, and we do not see how this could have introduced any bias into our results since we have included a series of cases first registered with the Edinburgh psychiatric service prior to July 1975. However, the method used might have missed some patients. Any patient admitted before 1969 but who remained well between January 1970 and March 1987 would not appear in the case register, and hence would not be included. However, the number is likely to be small, and the vast majority would not have been prescribed lithium (since only 65 patients were taking it by 1970). So the exclusion of such good prognosis patients from the control group would tend to bias the results in favour of lithium.

The main conclusion from this study is that lithium prophylaxis in bipolar patients who have had two episodes in two years or three episodes in five years does not confer the statistically significant benefit that would be anticipated from prospective clinical trials. This study reflects what is happening in ordinary clinical practice, and its implications are important and serious, especially since the group we have selected for study, i.e. that with several previous episodes of illness, is the group that has been identified as the most likely to respond in prospective studies (Bouman *et al*, 1986).

Those patients who took lithium for at least six months following the index episode were included in the treatment group. Thus, if patients stopped their lithium soon after, they still remained in this group until the next relapse or until the end of the study period. It could be argued that the results have been influenced by early discontinuation, although only 8 of the 41 patients in the treatment group were

TABLE II
Admission rates and annual duration of hospitalisation, lithium group v. *controls*

Characteristic	*Lithium group* n = *41*	*Control group* n = *40*[1]	*Significance*[2]
Total admissions per year of follow-up	12.5	14.9	Combined mean 0.34 $\chi^2 = 0.59$ NS
Period spent as an in-patient: weeks (annual mean)	2.17	2.65	Combined mean 2.41 $\chi^2 = 0.30$ NS

1. Two patients were excluded because of insufficient data.
2. χ^2 corrected for continuity.

known to have discontinued the lithium within two years. Despite this, it is possible that the patients had taken lithium erratically and therefore not sustained adequate plasma levels after the first 6 months of follow-up, or else that they had discontinued it and become subject to withdrawal relapses (Mander & Loudon, 1988). Nevertheless, the intention of the clinicians was to treat this group, and this "analysis is therefore a genuine reflections of the success (or otherwise) of that decision" (Mander, 1986).

Patients on long-term lithium are closely supervised and therefore it is possible that they have a greater chance of being admitted to hospital for even minor recurrences of symptoms. Our study has not examined the two groups for differences in the severity of symptoms during relapses, but there was no difference in the length of in-patient stay or in the total number of admissions during the follow-up period.

Admission to hospital depends not only on the severity of an illness but also on other factors, such as the degree of social support available, the attitudes of the patients and their relatives, admission policy, experience of the psychiatrists, etc. We would expect such factors to influence both treatment and control groups equally, but we have not been able to study this in detail.

Symonds & Williams (1981) stated that there was the possibility of misinterpretation of symptoms and atypical conditions receiving the diagnostic label of hypomania, in order to justify the use of long-term lithium. We tried to ensure that the symptoms recorded by medical staff corresponded with nursing reports and previous admission notes, but since clinical notes sometimes reflect the clinician's bias towards a particular diagnosis, such an error cannot be ruled out.

The best follow-up study so far rated only 33% of bipolar patients as good responders to lithium (Prien *et al*, 1984). Since only 50% of the original group who were prescribed lithium took it for the entire follow-up period, it is reasonable to conclude that only 16% of the 'intention to treat' group did well. In our view it is this minority of bipolar patients who respond to prophylactic lithium. Unfortunately, the current trend is to use it for all patients with this diagnosis, often indefinitely, and sometimes despite a clear lack of effect.

Although there was a reduction of 16% in the annual rate of admissions and 18% in the annual mean time spent as an in-patient, neither of these reached statistical significance. Similarly, there was no significant difference in the life table curves, although the small numbers between two and six years could have led to a type II error. Therefore there may be an improved outcome in a small number of patients who take lithium for longer than two years. It is important to emphasise that only two patients remained well throughout the study, and they were both taking lithium – a clinically important minority.

Lithium surveillance in Edinburgh is monitored by general practitioners in the majority of patients. Supervision by the lithium clinic consists of written reminders for serum estimations to be undertaken. It has been suggested by Masterton *et al* (1988) that follow-up by general practitioners may be less effective compared with psychiatric/lithium clinic follow-up. We would be interested to see whether similar studies, where lithium clinics operate, result in an improved performance for lithium prophylaxis, which presumably might occur because of better long-term compliance.

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References

Angst, J., Dittrich, A. & Grof, P. (1969) Course of endogenous affective psychoses and its modification by prophylactic administration of imipramine and lithium. *International Pharmacopsychiatry*, **2**, 1–11.

American Psychiatric Association (1980) *Diagnostic & Statistical Manual of Mental Disorders* (DSM–III). Washington DC: APA.

Baastrup, P. C., Poulson, J. C., Schou, M., *et al* (1970) Prophylactic lithium: double blind discontinuation in manic depressive disorders. *Lancet*, *ii*, 326–360.

Baldessarini, R. J. (1970) Frequency of diagnosis of schizophrenia versus affective disorders from 1944 to 1968. *American Journal of Psychiatry*, **127**, 759–763.

Bouman, T. K., Niemantsverdriet-Van Kampan, J. G., Ormel, J. *et al* (1986) The effectiveness of lithium prophylaxis in bipolar and unipolar depressions and schizoaffective disorders. *Journal of Affective Disorders*, **11**, 275–280.

Cade, J. F. J. (1949) Lithium salts in the treatment of psychotic excitement. *Medical Journal of Australia*, **2**, 349–352.

Coppen, A., Noguera, R., Bailey, J., *et al* (1971) Prophylactic lithium in affective disorders – a controlled trial. *Lancet*, *ii*, 275–279.

Dickson, W. E. & Kendell, R. E. (1986) Does maintenance lithium therapy prevent recurrences of mania under ordinary clinical conditions. *Psychological Medicine*, **16**, 521–530.

Fleiss, J. L., Dunner, D. L., Stallone, F. & Fieve, R. R. (1976) The Life Table – a method for analysing longitudinal studies. *Archives of General Psychiatry*, **33**, 107–112.

Grof, P. (1987) Admission rates and lithium therapy. *British Journal of Psychiatry*, **150**, 264–265.

——, Schou, M., Angst, M., *et al* (1970) Methodological problems of prophylactic lithium in recurrent affective disorders. *British Journal of Psychiatry*, **116**, 599–619.

Hullin, R. P., McDonald, R. & Allsopp, M. N. E. (1972) Prophylactic lithium in recurrent disorders. *Lancet*, *i*, 1044–1046.

Mander, A. J. (1986) Is lithium justified after one manic episode? *Acta Psychiatrica Scandinavica*, **73**, 60–67.

—— & Loudon, J. B. (1988) Rapid recurrence of mania following abrupt discontinuation of lithium. *Lancet*, *ii*, 15–17.

Masterton, G., Warner, M. & Roxburgh, B. (1988) Supervising lithium – a comparison of a lithium clinic, psychiatric out-patient clinic and general practice. *British Journal of Psychiatry*, **152**, 535–538.

Parker, H., O'Donnell, M. & Walter, S. (1985) Changes in the diagnosis of the functional psychoses associated with the introduction of lithium. *British Journal of Psychiatry*, **146**, 377–382.

Prien, R. F., Caffey, E. M. & Klett, C. J. (1973) Prophylactic efficacy of lithium carbonate in manic–depressive illness. *Archives of General Psychiatry*, **28**, 337–341.

——, Kupfer, D. J., Mansky P. A., *et al* (1984) Drug therapy and the prevention of recurrences in unipolar and bipolar disorders. *Archives of General Psychiatry*, 41, 1096–1104.

Symonds, R. L. & Williams, P. (1981) Lithium and the changing incidence of mania. *Psychological Medicine*, **11**, 193–196

Siegel, S. (1956) *Non-Parametric Statistics in Behavioural Science*. Tokyo: McGraw Hill.

Tyrer, S. P. (1985) Lithium in the treatment of mania. *Journal of Affective Disorders*, **8**, 251–257.

World Health Organization (1978) *Mental Disorders: Glossary and Guide to their Classification in Accordance with the Ninth Revision of the International Classification of Diseases* (ICD–9). Geneva: WHO.

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The Measurement of Transmembrane Cation Transport *in vivo* in Acute Manic Illness

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We have used a novel technique to assess the transport of cations across the erythrocyte membrane *in vivo* in unmedicated patients suffering an acute manic illness. The results show that erythrocyte cation transport via the sodium-pump enzyme Na^{+},K^{+}-ATPase is increased in manic patients compared with healthy controls.

Episodes of mania are the diagnostic hallmark of bipolar affective illness. Several biochemical mechanisms which might be important in the pathogenesis of affective illness have been investigated in patients suffering from episodes of mania, and one area of interest has been alterations in the transport of cations across cell membranes. Specifically, several groups of investigators have demonstrated an alteration in the *in-vitro* activity of the enzyme sodium- and potassium-activated adenosine triphosphatase (Na^{+},K^{+}-ATPase) in the membranes of the erythrocytes and platelets of patients suffering from episodes of mania. However, the results of these studies have been conflicting. Some workers have shown a decrease in Na^{+},K^{+}-ATPase activity during episodes of acute mania (Hokin-Neaverson *et al*, 1974; Naylor *et al*, 1980) or an increase in enzyme activity on recovery from a manic illness (Naylor *et al*, 1976). In contrast, other groups have found an increase in Na^{+},K^{+}-ATPase activity in patients suffering from a manic episode (Sengupta *et al*, 1980; Akagawa *et al*, 1980; Nurnburger *et al*, 1982). The reasons for the discrepancies between the results of these studies are not clear, but may relate to differing diagnostic criteria for patients included in the studies, the effects of medication given to acutely disturbed patients before testing, or the *in-vitro* assays used to assess Na^{+},K^{+}-ATPase activity.

Boon *et al* (1984) reported a technique which allows the assessment of cation transport *in vivo*. This technique is based on the measurement of plasma and erythrocyte rubidium concentrations after the oral administration of a dose of rubidium chloride. They subsequently showed changes in *in-vivo* rubidium transport in patients suffering from essential hypertension, or chronic renal failure, and after the short-term administration to volunteers of the Na^{+},K^{+}-ATPase inhibitor digoxin (Boon *et al*, 1984; Boon *et al*, 1986). They showed that erythrocyte rubidium uptake *in vivo* can be inhibited not only by the prior administration of digoxin but also by the *ex-vivo* incubation of pre-loaded whole blood in the presence of digoxin (Wood *et al*, 1988*a*), and these results suggest that the majority of the accumulation of rubidium by erthrocytes *in vivo* during the period of study is attributable to the cation-transporting activity of Na^{+},K^{+}-ATPase.

We have, therefore, used this technique to assess cation transport *in vivo* in a group of patients suffering an episode of manic illness, and who received no psychotropic medication before or during the study.

Method

Patients

We studied six patients shortly after their admission to hospital. All had been referred to one of the psychiatric hospitals in Oxford and were assessed by two psychiatrists, who agreed on a diagnosis of a manic episode requiring in-patient management. All the patients also met the DSM-III criteria for an acute episode of mania (American Psychiatric Association, 1980).

Three patients were admitted for a first episode of mania. None of these three patients had had previous episodes of affective illness, and so none was taking any regular prophylactic psychotropic medication at the time of admission. The other three patients had suffered previous episodes of mania or depression (or both). Two of the three patients had also received prophylactic lithium. None of the three received psychotropic drugs for at least one year before admission. All six patients were managed without drug treatment, apart from a single night-time dose of a benzodiazepine, from the time of their admission to the time of rubidium administration. Rubidium administration began within 18 hours of admission in all patients.

Control subjects

We compared the patients with healthy volunteers who had no personal or close family history of affective illness, and who were taking no regular medication. These healthy

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volunteers were individually matched with manic subjects for age, weight, and sex.

Study protocol

The protocol for the study was approved by the Psychiatric Sector Ethics Committee of the Oxfordshire Health Authority. Shortly after clinical assessment on the day of admission the patients were interviewed, and the nature and details of the test were explained. They were approached again on the following morning and, if they were still willing to take part in the study, testing began immediately.

The patients and control subjects received an oral dose of rubidium chloride dissolved in tap water (Boon *et al*, 1984). The total dose of rubidium chloride was 8 mg/kg body weight, and this was given in eight separate doses of 1 mg/kg at intervals of 15 minutes. Samples of venous blood were taken immediately before the start of the rubidium load test, and one hour and five hours after the last dose of rubidium. The plasma and erythrocytes were separated by centrifugation at 4°C, and plasma and erythrocyte rubidium concentrations were measured by atomic absorption spectrophotometry using a Perkin Elmer 2380 spectrophotometer incorporating an HG 400 graphite furnace (Perkin-Elmer, Beaconsfield, Bucks). Analytical-grade rubidium chloride was obtained from British Drug Houses (Athelstone, Warwickshire).

In-vivo cation transport was assessed as the change in plasma and erythrocyte rubidium concentrations after the oral administration of rubidium chloride. In addition, the rate of uptake of rubidium by erythrocytes was calculated as the rate of increase in erythrocyte rubidium concentrations between one hour (RBC1) and five hours (RBC5), and corrected for the plasma rubidium concentration by dividing it by the plasma rubidium concentration at one hour (plasma1). Thus, rate of Rb uptake $= (Rb_{RBC5} - Rb_{RBC1})/4 + Rb_{Plasma1}$. This value has the units of a rate constant (h^{-1}) and we refer to it as a pseudo-rate constant.

Plasma and intra-erythrocytic potassium concentrations and serum creatinine and urea were also measured in all the subjects in samples taken immediately before the rubidium load test.

During the period of rubidium loading the symptoms of mania were rated by one of us (AJW) using the Young Rating Scale for Mania (Young *et al*, 1978).

Differences in the results of cation concentration measurements were assessed stastically using Student's *t*-test for normally distributed paired data, these data being expressed as means with standard deviations. Data that were not normally distributed have been expressed as medians and ranges and have been assessed by the signed-rank test for paired data.

Results

The demographic data and results of *in vivo* cation transport measurement are shown in Table I. There was no significant difference in either age or weight between the two groups.

TABLE I
Demographic data and results of in vivo *cation transport measurement in acutely manic and matched control subjects*

	Acute mania	*Control*
Age range: years	21–75	24–65
Weight: mean (range) (kg)	70 (65–80)	72 (64–95)
In vivo cation transport (means ± s.d.)		
increment in plasma Rb conc. (μmol/l) (mean ± s.d.)		
1 h	9.13 ± 1.00	8.72 ± 1.60
5 h	6.67 ± 0.85	5.79 ± 1.30
increment in erythrocyte Rb conc. (μmol/l) (mean ± s.d.)		
1 h	29.46 ± 6.02	17.27 ± 3.96*
5 h	49.75 ± 10.9	32.70 ± 5.22*
pseudo rate constant (h^{-1})	0.48	0.33
(median range)	(0.35–0.65)	(0.26–0.42)*
Potassium concentrations (mmol/l) (mean ± s.d.)		
plasma	4.87 ± 0.33	4.48 ± 0.51
erythrocyte	87.51 ± 4.15	84.02 ± 5.08

*$P < 0.05$.

The median Young score for the patients was 23 (range 22–30). This implies a significant disturbance of behaviour but does not identify any particular subgroup of manic patients.

There was a significant increase in the intraerythrocytic rubidium concentration in the manic patients at both 1 h and 5 h after the rubidium load. The pseudo rate constant for rubidium uptake into erythrocytes was also significantly higher in the manic patients than in the matched controls ($P < 0.05$).

There was no significant difference in the plasma concentrations of rubidium after rubidium loading.

Because potassium and rubidium compete *in vivo* for transport by the Na^+,K^+-ATPase it is important to measure plasma and erythrocyte potassium concentrations in studies of this kind. There were no significant differences in these parameters between the two groups (Table I). All subjects had normal creatinine and urea concentrations (data not shown).

Discussion

There was a significantly greater intra-erythrocytic concentration of rubidium in patients than in controls, and the pseudo-rate constant for erythrocyte rubidium uptake was also significantly increased in the manic patients. Previous studies using this *in vivo* protocol have shown that the majority of erythrocyte rubidium uptake *in vivo* is mediated by Na^+,K^+-ATPase (Boon *et al*, 1984; Wood *et al*, 1988*a*), and we conclude that the changes shown here are consistent with an increase in the *in vivo* activity of erythrocyte Na^+,K^+-ATPase in acute manic illness.

However, it is possible that the increased uptake of rubidium into erythrocytes might result not from increased Na$^+$mK$^+$-ATPase activity but either from decreased efflux of rubidium from the cell or from increased uptake via some other pathway, such as the loop diuretic-sensitive Na/K cotransporter. Both passive rubidium efflux from cells and Na/K cotransport activity have been studied *in vitro* in the erythrocytes of patients with manic–depressive illness by Dagher *et al* (1984). They found no change in either cotransport activity or passive permeability, and this suggests that the increased rubidium uptake we have seen *in vivo* is due principally to an increase in Na$^+$,K$^+$-ATPase activity.

This finding is in agreement with the results of some *in-vitro* studies in manic patients (e.g. Sengupta *et al*, 1980), but conflicts with other, usually either, studies which demonstrated either a reduction in Na$^+$,K$^+$-ATPase activity during mania or an increase in activity following clinical recovery from a manic episode (e.g. Naylor *et al*, 1976). The reason for this difference is not clear, but it may reflect the fact that many of the patients included in the earlier studies were receiving medication, or it may be due to a difference in the severity of illness suffered by the patients included in the various studies previously undertaken.

The discrepancies between earlier *in-vitro* studies may also result from minor differences in the techniques used. All the *in-vitro* techniques involve repeated centrifugation, cooling, rewarming, and washing of the cells before being assayed. These manipulations might themselves have effects upon cellular cation concentrations or upon the activity of Na$^+$,K$^+$-ATPase, and they would inevitably remove plasma-borne factors which might be important in the physiological regulation of the sodium pump enzyme (deWardener & Clarkson, 1985). These technical limitations of the *in-vitro* assays re-emphasise the value of the *in-vivo* technique used in the present study.

The patients included in this study had Young mania rating scores in the range 22–30. This suggests a significant manic episode (not hypomania), but does not specify any particular pattern of symptoms. In fact, most of the patients were elated and had significant loss of insight. However, they were in the subgroup of manic individuals who are industrious and co-operative. They were neither particularly irritable nor extremely overactive. In fact, all were able to stay in a single room with the investigator throughout the two hours of rubidium administration. This may be important, in view of the changes in intra-erythrocytic cation concentrations which have been described following brief strenuous exercise (Bodemann *et al*, 1982), and which have been interpreted as being due to a change in Na$^+$, Ka$^+$-ATPase activity during exercise.

The mechanism whereby erythrocyte rubidium uptake is increased in manic illness is not known, nor is it possible to deduce the mechanism from the results of the present study. The potential role of the vanadate ion (the +5 oxidation state of vanadium) in the regulation of Na$^+$,K$^+$-ATPase activity in affective illness has been emphasised by Naylor & Smith (1981), and has recently been reviewed by Wood (1987). However, the present study would not support the suggestion (Dick *et al*, 1982; Naylor *et al*, 1984) that there is *decreased* activity of Na$^+$, K$^+$-ATPase due to increased vanadium concentrations in manic patients. Nevertheless, the changes in vanadium concentrations and in intracellular vanadium handling in affective illness are still poorly understood (see Wood, 1987), and the more recent work of Naylor *et al* (1987*a,b*) has stressed a possible role for vanadium in the *depressive* pole of affective illness, in which most *in-vitro* studies suggest a decrease in Na$^+$,K$^+$-ATPase activity.

It is possible that the concentration of some plasma-borne regulator of Na$^+$,K$^+$-ATPase is changed in manic illness. The possible effect of exercise and circulating catecholamines on Na$^+$,K$^+$-ATPase activity have been discussed in two reports (Bodemann *et al*, 1982, 1985), and may be relevant to the changes in physical activity and arousal during periods of affective illness as mentioned above. However, we have investigated the effect of the β_2-adrenoreceptor agonist salbutamol on rubidium uptake *in vivo* using the oral rubidium load, and have shown no stimulation of erythrocyte rubidium uptake (Wood *et al*, 1988*a*). Previous studies have shown that adrenoreceptor-mediated catecholamine stimulation may be important in the regulation of Na$^+$, K$^+$-ATPase activity in the brain (Phillis & Wu, 1981).

Many other circulating substances, including angiotensin, corticosteroids, thyroxine, and α-adrenoreceptor agonists, have been shown to modulate Na$^+$,K$^+$-ATPase activity in a number of tissues, and clearly an alteration in the circulating concentrations of any combination of these might underlie our present results.

It is also possible that the change in Na$^+$, K$^+$-ATPase activity is one manifestation of a more generalised change in membrane structure or function in manic illness. Some evidence for this comes from the work of Pettegrew *et al* (1982), who have inferred an alteration in membrane structure of both the erythrocytes and the lymphocytes of patients with manic–depressive illness.

The profile of plasma rubidium concentrations after oral rubidium administration is not altered in manic patients. This suggests that the increased rate of rubidium uptake into erythrocytes occurs only into a small intracellular volume, since a more generalised increase in tissue rubidium uptake ought to lead to an observable increase in the rate of clearance of rubidium from the plasma. Hence, the changes we have found in erythrocyte Na^+, K^+-ATPase activity cannot be assumed to reflect changes occurring in any other specific organ, including the brain. The direct study of cation transport *in vivo* in neurons is obviously desirable but must await the development of suitable and sensitive non-invasive techniques, such as nuclear magnetic resonance spectroscopy.

Conclusions

We have found an increase in the rate of uptake of rubidium into erythrocytes *in vivo* in unmedicated patients suffering from an acute manic illness. These patients fulfilled strict diagnostic criteria for acute mania, were suffering a significant symptomatic illness at the time of testing, and had received no medication before being studied. The changes we have found suggest that there is an increase in the *in-vivo* activity of Na^+,K^+-ATPase in the erythrocyte membrane in acute manic illness. This *in-vivo* model offers an extension of the *in-vitro* measurements of Na^+,K^+-ATPase activity used in previous studies. However, our data suggest that changes demonstrated in the erythrocyte membrane *in vivo* cannot necessarily be extrapolated to infer any similar changes in cation transport in the brain.

For acknowledgements, references and authors' details, see the following paper, on pp. 504–510

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The Effect of Lithium on Cation Transport Measured *in vivo* in Patients Suffering from Bipolar Affective Illness

A. J. WOOD, M. ELPHICK, J. K. ARONSON and D. G. GRAHAME-SMITH

We have investigated cation transport *in vivo* in patients being treated with lithium for bipolar affective illness by studying the disposition of rubidium after an oral load of rubidium chloride. The rate of erythrocyte cation transport was increased in the patients when compared with matched healthy volunteers. However, the rate of *in-vivo* erythrocyte rubidium accumulation in the euthymic treated patients was significantly lower than in a matched group of unmedicated manic patients. The regulation of specific pathways for cation transport may be altered in individuals predisposed to affective illness.

The specific therapeutic activity of lithium salts was first described in a group of manic men by Cade (1949). His discovery was made as a result of chance observations, and, despite almost 40 years of investigation of the effects of lithium on many aspects of neuronal biochemistry and neurotransmitter function, the pharmacological actions crucial to its well established clinical effects are not yet known (Wood & Goodwin, 1987).

One area of interest has been the changes in the transport of cations across cell membranes which occur in patients suffering from affective illness. Alterations in the activity of the sodium-pump enzyme Na^+,K^+-ATPase have been described *in vitro* by many groups of investigators in both the manic and depressive poles of bipolar illness. Most studies of depressed patients have shown reduced Na^+,K^+-ATPase activity during periods of illness. However, *in-vitro* studies in acute manic illness have been much less clear. Early studies suggested decreased Na^+,K^+-ATPase activity in periods of mania, but more recent studies have demonstrated increased enzyme activity in this group (Naylor *et al*, 1973; Hokin-Neaverson *et al*, 1974; Naylor *et al*, 1976; Hesketh *et al*, 1977; Sengupta *et al*, 1980). Our own *in-vivo* study has recently demonstrated an increase in erythrocyte Na^+,K^+-ATPase in patients suffering from an acute manic illness (Wood *et al*, 1987, and see preceding paper).

The potential importance of these changes in cation transport to the treatment of bipolar affective illness has also been investigated (for a review see Wood, 1987). The effect of lithium salts on cation transport via Na^+,K^+-ATPase was first studied *in vitro* by Naylor *et al* (1974), who showed an increase in the activity of Na^+,K^+-ATPase in the erythrocyte membranes of patients taking lithium salts (in a double-blind comparison with inactive placebo). Other investigators have also shown an increase in Na^+,K^+-ATPase activity *in vitro* in erythrocyte and platelet membranes from patients on long-term lithium therapy (Hokin-Neaverson *et al*, 1976; Hesketh *et al*, 1978; Sengupta *et al*, 1980). Furthermore, in one study there was demonstrated an inverse correlation between the degree of stimulation of Na^+K^+-ATPase by lithium and the risk of subsequent clinical relapse (Johnston *et al*, 1980). However, some workers have failed to show any effect of lithium on Na^+,K^+-ATPase *in vitro* (Nurnburger *et al*, 1982; Dagher *et al*, 1984; Thakar *et al*, 1985).

When studies of this sort are conducted on patients responding to and subsequently being maintained on lithium, it is impossible to say whether the observed change in sodium-pump activity is a *direct* action of lithium on Na^+,K^+-ATPase, or whether it is a *secondary* consequence of a change in the patient's mental state mediated by some other mechanism. This difficulty can be avoided by studying the effect of lithium on cation transport in healthy volunteers (in whom no change in mental state would be expected after lithium administration). In the single *in-vitro* study of the effect of lithium on Na^+,K^+-ATPase activity in healthy volunteers, Naylor *et al* (1977) showed no change in erythrocyte Na^+,K^+-ATPase activity after 14 days of lithium treatment. However, we have used a technique for studying Na^+,K^+-ATPase activity *in vivo*, and have found a stimulation of the activity of erythrocyte Na^+,K^+-ATPase in volunteers who had received lithium for 21 days, suggesting that there is a *direct* stimulatory effect of lithium on the activity of erythrocyte Na^+,K^+-ATPase *in vivo* (Wood *et al*, 1986).

In the present study we have used this *in-vivo* technique to study cation transport in patients with manic–depressive illness. We have compared the results in a group of euthymic patients receiving long-term treatment with lithium as prophylaxis for bipolar affective illness with those in a group of untreated acutely manic patients, in order to investigate further the effect of lithium on cation transport *in vivo* and in order to assess the possible relevance of any change in cation transport *in vivo* to the therapeutic properties of the drug.

Methods

Subjects

Lithium-treated patients

We recruited ten patients (six men, four women) from the specialist lithium clinic in Oxford. All were receiving lithium for the prophylaxis of an affective illness, which had included at least one manic episode (hence bipolar affective illness), and had been taking lithium for at least six months before the study. All were being seen regularly for assessment of their symptoms and for monitoring of their lithium treatment, and all had stable serum lithium concentrations within the range 0.4–1.0 mmol/l, suggesting good compliance with therapy. All were out-patients at the time of testing, and were taking no other drugs. Symptoms of depression were rated clinically using the Beck or Hamilton rating scales (Hamilton, 1960; Beck *et al*, 1961). The symptoms of mania were also assessed using the Young Mania Rating Scale (Young *et al*, 1978).

Acutely manic patients

For the purposes of comparison, as detailed in the results section, we have included data from five patients with an acute manic illness, who were recruited to a separate study. This group was recruited shortly after their admission to hospital. The diagnosis according to the DSM–III criteria (American Psychiatric Association, 1980) was agreed by two psychiatrists. The patients received no psychotropic medication before or during testing. The symptoms of mania were assessed during the test period using the Young Mania Rating Scale (Young *et al*, 1978). A full description of this study is published elsewhere (Wood *et al*, 1987, and see preceding paper). The Young ratings were in the range 22–31 for the five patients.

Controls

Comparison was made with healthy volunteers matched for age, sex, and weight, who had no history of affective illness, and who were taking no drugs at the time of the study.

Study protocol

On the day of the study all the subjects received a loading dose of rubidium, according to the protocol of Boon *et al* (1984) (and see previous paper for details). All tests started at 9 a.m. Samples of venous blood were taken immediately before the first dose and at one hour and five hours after the last dose of RbCl for the measurement of plasma and erythrocyte rubidium concentrations.

In order to assess the linearity of uptake of rubidium into erythrocytes in the presence of lithium, three of the patients took a second rubidium load (at least six months after the first). On the second occasion blood samples were taken hourly between one hour and five hours after the rubidium load, and rubidium concentrations were measured in the usual way.

The patients were taking a variety of lithium carbonate formulations and continued to take their lithium according to the prescribed schedule before and throughout the day of the test. The 12-hour serum lithium concentration was measured on the day of the rubidium test, both to assess continued compliance with therapy and to confirm that lithium concentrations were within the accepted therapeutic range.

TABLE I

Demographic data and the results of in-vivo *cation transport assay in 10 patients receiving long-term lithium as prophylaxis for bipolar affective illness, and in matched controls*

	Euthymic patients	*Controls*
Number	10	10
Age: years (means range)	45 (23–66)	44 (26–67)
Weight: kg (means range)	74 (61–90)	69 (60–95)
Serum Li conc.: mmol/l (means range)	0.82 (0.5–1.08)	
Symptom assessment (medians, range)		
Beck scale	4 (0–11)	
Hamilton scale	4 (1–5)	
Young scale	0 (0–2)	
Increment in plasma Rb conc.: μmol/l		
1 hour	10.18 (1.65)	11.52 (2.44)
5 hours	5.29 (1.28)	7.69 (4.29)
Increment in erythrocyte Rb conc.: μmol/l		
1 hour	26.07 (7.61)	27.69 (6.15)
5 hours	43.68 (10.5)	42.40 (7.73)
Pseudo-rate constant: h^{-1} medians (IQR), range)	0.35 (0.30–0.38)	0.24 (0.17–0.34)*
Potassium conc. mmol/l (means, s.d.)		
plasma	4.93 (1.01)	4.80 (0.67)
erythrocytes	81.92 (4.14)	84.17 (4.16)
Sodium conc. mmol/l (means, s.d.)		
plasma	140.8 (5.62)	141.9 (5.65)
erythrocytes	10.01 (4.61)	8.01 (0.67)

*$P<0.02$.

The concentrations of sodium and potassium in both the plasma and erythrocytes were also measured, in blood taken immediately before the adminstration of rubidium. The method of data analysis was as detailed in the previous paper (p. 501).

Results

The demographic details of the euthymic patients and the matched healthy volunteers are shown in Table I. There were no significant differences in ages or weights between the two groups, and all the subjects had normal blood pressures measured by sphygmomanometry (data not shown). No patient was rated as currently suffering from a significant affective episode by clinician-rated symptom scores. The one patient who scored highly on the self-rated Beck inventory had on the previous day taken his eldest daughter away to boarding school for the first time. He felt that his high score was directly related to that episode, and the self-reporting Beck scores measured at routine clinical assessment were normal both before and after this single high rating.

Although the plasma concentrations were lower at both one hour and five hours, and the increase in erythrocyte rubidium concentrations over the time of testing was greater in the patients, none of these differences achieved statistical significance (Table I). However, the differences were reflected in the pseudo-rate constant for rubidium uptake into the erythrocytes, which was significantly increased in the patients receiving lithium therapy when compared with the control group (Table I). There was no correlation between the pseudo-rate constant for rubidium uptake into erythrocytes and: the serum lithium concentration; the duration of lithium treatment; or the age of the patient.

The uptake of rubidium into the erythrocyte was linear over the period of the *in-vivo* test. The data for the three patients retested in this way are shown in Fig. 1.

The concentrations of potassium in both the plasma and the erythrocytes were similar in the two groups. Although there was a trend towards a higher intra-erythrocytic sodium concentration in the euthymic patients on lithium (mean 10.01 mmol/l in patients v. 8.01 mmol/l in controls) this difference did not achieve statistical significance. The plasma sodium concentration was similar in the two groups.

In order to assess further the changes in rubidium handling between untreated manic patients and euthymic patients taking lithium, each lithium-treated euthymic patient was paired with the manic patient matched most closely for age and weight, and the results of *in-vivo* rubidium loading were compared ($n=5$). It must be emphasised that these two groups were not originally selected to be matched populations. There was no significant difference in the mean age or weight of these two groups. The pseudo-rate constant for rubidium uptake into erythrocytes was significantly lower in the subgroup of the euthymic, lithium-treated patients (median 0.29, range 0.26–0.55) than in the matched, unmedicated, acutely manic group (median 0.48, range 0.35–0.65) ($P<0.05$) by signed-rank test). The individual data for the changes in the

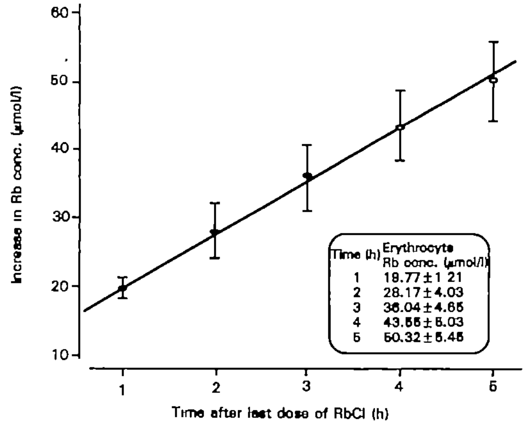

FIG. 1 The time course of the uptake of rubidium into erythrocytes in three euthymic patients taking lithium as prophylaxis for bipolar affective illness. Rubidium concentrations are shown as mean ±s.d.

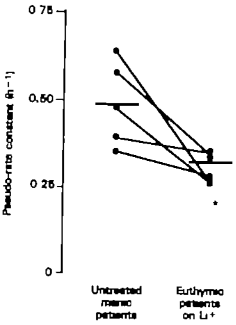

FIG. 2 A comparison of the pseudo-rate constant for rubidium uptake into erythrocytes between five unmedicated manic patients and five euthymic patients taking long-term lithium therapy for bipolar affective illness. The pseudo-rate constants (h^{-1}) are shown as the median values (horizontal bars) and the individual changes for each paired comparison. *$P<0.05$ by signed-rank.

pseudo-rate constant between the matched pairs, as well as the group medians, are shown in Fig. 2.

Discussion

Increased erythrocyte Na^+,K^+-ATPase in euthymic patients taking lithium

The results of this study show an increase in the rate of rubidium uptake into erythrocytes, as reflected in the pseudo-rate constant, in patients with a history of affective illness, currently well and taking long-term lithium, when compared with healthy controls. Our previous work using this *in-vivo* test shows that the increase in erythrocyte rubidium uptake reflects an increase in the *in-vivo* activity of Na^+,K^+-ATPase in the erythrocyte membrane (Boon, 1984; Wood *et al*, 1988*a*). Hence we conclude that there is an increase in the cation-transporting properties of Na^+,K^+-ATPase in euthymic patients taking lithium. This is consistent with the results of some of the earlier *in-vitro* studies of the effect of lithium on Na^+,K^+-ATPase in patients (Naylor *et al*, 1974; Hokin-Neaverson *et al*, 1976; Hesketh *et al*, 1978).

Possible mechanisms for the stimulation of Na^+,K^+-ATPase by lithium

The mechanism of the stimulation of Na^+,K^+-ATPase *in vivo* by lithium is not clear. It is possible that the stimulation occurs as a consequence of an alteration in catecholamine function, which has been found in the brain after lithium treatment (see Wood & Goodwin, 1987). Such an effect of catecholamines on Na^+,K^+-ATPase via β_2-adrenoceptors has been demonstrated in patients following acute myocardial infarction, and is thought to underlie the hypokalaemia often seen in this group (Brown *et al*, 1983; Clausen & Flatman, 1980; Baron *et al*, 1985). However, in the periphery the major effect of lithium on adrenergic function is probably an uncoupling of receptor stimulation from the production of cyclic adenosine monophosphate by adenylate cyclase (Ebstein *et al*, 1976), and the predicted result of this uncoupling would be an inhibition of Na^+,K^+-ATPase activity. Furthermore, our own studies using the *in-vivo* rubidium load have shown no change in Na^+,K^+-ATPase activity in the erythrocyte after the administration of the β_2-adrenoceptor agonist drug salbutamol to healthy volunteers, and this suggests that an effect of catecholamines is not important in *in-vivo* changes in cation transport in erythrocytes measured in this way (Wood *et al*, 1988*a*).

It has also been suggested that lithium stimulates Na^+,K^+-ATPase by protecting the enzyme from inhibition by the vanadate ion. Such a protective effect of lithium salts has been shown in the erythrocyte *in vitro* (Naylor *et al*, 1981) and has subsequently also been demonstrated for the anticonvulsant carbamazepine, which is increasingly being used in the prophylactic management of affective illness (Naylor, 1985).

Naylor *et al* (1977) observed that the intra-erythrocytic concentration of sodium is significantly increased in subjects taking lithium, and a raised intracellular sodium concentration is known to be stimulus to Na^+,K^+-ATPase activity. It may be, therefore, that lithium acts in some unknown way to raise intracellular sodium concentrations, and that the stimulation of Na^+,K^+-ATPase is a secondary adaptive response. In contrast, a direct stimulation of Na^+,K^+-ATPase by intracellular lithium would be expected to lead to a decrease in the intracellular sodium concentration. There was an increase in the intra-erythrocytic sodium concentration in patients taking lithium in the present study, but it did not reach statistical significance (Table I). However, this may reflect the relatively small number of subjects tested as well as the relatively large variance in the intra-erythrocytic sodium concentrations measured in the patient group.

The similarity in the potassium concentrations in the plasma and cells from the patients and controls suggests that changes in the potassium:rubidium concentration ratio, and hence the relative substrate competition of the two ions for transport via Na^+,K^+-ATPase, is not likely to explain the difference in rubidium uptake between the two tested groups.

The kinetics of rubidium uptake

Our measurement of the rate of rubidium uptake *in vivo* and the derivation of the pseudo-rate constant is likely to be a true reflection of the rate constant for uptake, but this can only be assumed because the extracellular rubidium concentrations remain relatively low throughout the test. Even under these conditions, the rate constant for the uptake process is a function of the ratio between the two parameters of the transport system, V_{max} (the maximal rate of uptake under conditions of substrate saturation) and K_m (a measure of the affinity of the enzyme for rubidium ions) (Aronson, 1989). It is possible that the observed change in the pseudo-rate constant for rubidium uptake is the net result of a combination of changes in V_{max} and K_m. The direction of the changes in the individual parameters cannot be deduced from our data. Individual measurement of these two parameters would be possible in an *in-vitro* assay, but such studies have not previously been undertaken.

For the three patients who agreed to take a second rubidium load it was possible to confirm that the uptake of rubidium into erythrocytes was linear in the presence of therapeutic concentrations of lithium (Fig. 1). This is clearly an important precondition for the calculation of the pseudo-rate constant for rubidium uptake as described above. Furthermore, it excludes the possibility of any complex time- or rubidium-concentration-dependent action of lithium on the regulation of rubidium uptake via Na^+,K^+-ATPase during the period of the *in-vivo* test.

Despite the observed increase in the rate of rubidium uptake into the erythrocyte, we were not able to demonstrate any significant increase in actual intra-erythrocytic rubidium concentrations in patients. One explanation for this apparent discrepancy is that the plasma rubidium concentrations are lower at both one hour and five hours after the oral load, and that the fall in mean plasma concentration between one hour and five hours is greater in the patients (4.89 μmol/l) than in the control group (3.83 μmol/l). This increase in the clearance of rubidium from the plasma suggests that the rate of uptake of rubidium from the plasma into all tissues may have been greater in the lithium-treated patients. As a consequence of the increased clearance of plasma rubidium the erythrocytes might have been exposed to lower rubidium concentrations throughout the time of the uptake experiment, and a true increase in the *rate* of rubidium uptake into the erythrocyte might not therefore have been reflected in an actual increase in intra-erythrocytic rubidium concentrations.

The effect of lithium in manic illness: a synthesis of the *in-vivo* studies

The comparison of the pseudo-rate constant for erythrocyte rubidium uptake in acute manic illness and in euthymic lithium-treated patients suggests that there is actually a *fall* in cation transport activity *in vivo* during the symptomatic recovery of manic patients to a euthymic state. It is arguable that the untreated manic patients constitute a more appropriate control group for studying the dynamic change in cation transport after the treatment of affectively ill patients with lithium in order to make inferences about the mechanism of action of the drug in mania. The fall in rubidium uptake *in vivo* demonstrated here after the treatment of affectively ill patients with lithium does not support the hypothesis based on earlier studies, that the activity of Na^+,K^+-ATPase falls in mania and depression and increases as the illness remits or is successfully treated. In a separate investigation we have studied the effect of lithium upon Na^+,K^+-ATPase *in vivo* in healthy volunteers (Wood *et al*, 1986), and have demonstrated a stimulation of the enzyme in the group following 21 days of lithium treatment.

In an attempt to form an hypothesis to explain the effect of lithium in manic illness, we have combined the results of the above study with our present data and conclude that the successful treatment of mania with lithium is associated with a fall in cation transport *in vivo* to normal levels, but that lithium independently causes a direct stimulation of rubidium uptake via Na^+,K^+-ATPase (as this has been demonstrated in both patients and healthy volunteers). This explanation would imply that the crucial action of lithium in mania is not upon Na^+,K^+-ATPase. However, these results are equally well explained by the hypothesis that the Na^+,K^+-ATPase enzyme in the erythrocyte membrane of individuals predisposed to develop affective illness is functionally different from that of healthy volunteers, and that as one consequence of the difference it is inhibited after the administration of lithium, whereas the activity of 'normal' Na^+, K^+-ATPase found in healthy volunteers is increased by lithium ions.

Conclusions

We have shown stimulation of cation transport *in vivo* in euthymic patients taking lithium for the prophylactic management of bipolar affective illness, when compared with healthy controls, but a significant fall when compared with untreated manic patients.

There are two explanations compatible with these results. Firstly, that lithium has a direct stimulatory effect on erythrocyte Na^+,K^+-ATPase, but that this effect is independent of the antimanic action of the drug. Thus the demonstrated intermediate Na^+,K^+-ATPase activity in euthymic lithium-treated patients is the net result of a reduction in activity on return to a normal mental state and a direct stimulatory effect of lithium upon enzyme activity. Secondly, it is also possible that the Na^+,K^+-ATPase of patients at risk of developing affective illness is structurally and functionally different from the enzyme of healthy individuals, and that this abnormality causes it to respond differently to the presence of therapeutic concentrations of lithium. According to this model the intermediate enzyme activity in treated patients reflects a fundamentally different effect of lithium upon Na^+,K^+-ATPase in patients with manic–depressive illness.

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References

Akagawa, K., Watanabe, M. & Tsukade, Y. (1980) Activity of Na^+,K^+-ATPase in manic patients. *Journal of Neurochemistry,* **35**, 258–260.

American Psychiatric Association (1980) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn) (DSM–III). Washington, DC: APA.

Aronson, J. K. (1989) Methods for expressing the activity of transmembrane ion transport systems. *Clinical Science* (in press).

Baron, D. N., Green, R. J. & Khan, F. A. (1985) Adrenaline and ion flux in human leucocytes. *Clinical Science,* **68**, 517–521.

Beck, A. T., Ward, C. H., Mendelson, M., *et al* (1961) An inventory for measuring depression. *Archives of General Psychiatry,* **4**, 561–571.

Bodemann, H. H., Irmer, M. & Schluter, K. (1982) Catecholamines stimulate the NA,K-pump of human erythrocytes in vivo. *European Journal of Clinical Investigation,* **12**, 4.

——, ——, ——, *et al* (1985) Increased Na^+ transport in human red blood cells by beta adrenoceptor stimulation in vivo. In *The Sodium Pump* (eds I. Glynn & J. C. Ellory), pp. 721–722. London: Company of Biologists.

Boon, N. A., Aronson, J. K., Hallis, K. F., *et al* (1984) A method for the study of cation transport in vivo: effects of digoxin administration and of chronic renal failure on the disposition of an oral load of rubidium chloride. *Clinical Science,* **66**, 569–574.

——, ——, ——, *et al* (1986) Cation transport abnormalities in vivo in untreated essential hypertension. *Clinical Science,* **70**, 611–616.

Brown, M. J., Brown, D. C. & Murphy, M. B. (1983) $Beta_2$-receptor stimulation by circulating epinephrine causes prolonged hypokalemia. *New England Journal of Medicine,* **309**, 1414–1419.

Cade, J. F. (1949) Lithium salts in the treatment of psychotic excitement. *Medical Journal of Australia,* **36**, 349–352.

Clausen, T. & Flatman, J. A. (1980) B_2-adrenoceptors mediate the stimulating effect of adrenaline on active electrogenic Na–K transport in rat soleus muscle. *British Journal of Pharmacology,* **68**, 749–755.

Dagher, G., Gay, C., Brossard, M., *et al* (1984) Lithium, sodium and potassium transport in erythrocyte of manic depressive patients. *Acta Psychiatrica Scandinavica,* **69**, 24–36.

deWardener, H. E. & Clarkson, E. M. (1985) Concept of the natriuretic hormone. *Physiological Reviews,* **65**, 658–758.

Dick, D. A. T., Naylor, G. J. & Dick, E. G. (1982) Plasma vanadium concentration in manic and depressive illness. *Psychological Medicine,* **12**, 533–537.

Ebstein, R. P., Belmaker, R. H., Grunhaus, L., *et al* (1976) Lithium inhibition of adrenaline stimulated adenylate cyclase in humans. *Nature,* **259**, 411–413.

Hamilton, M. (1960) A rating scale for depression. *Journal of Neurology, Neurosurgery and Psychiatry,* **23**, 56–62.

Hesketh, J. E., Glen, A. I. M. & Reading, H. W. (1977) Membrane ATPase activity in depressive illness. *Journal of Neurochemistry,* **28**, 1401–1402.

——, Loudon, J. B., Reading, H. W., *et al* (1978) The effect of lithium treatment on erythrocyte membrane ATPase activities and erythrocyte ion content. *British Journal of Clinical Pharmacology,* **5**, 323–329.

Hokin-Neaverson, M., Spiegel, D. A. & Lewis, W. C. (1974) Deficiency of erythrocyte sodium pump activity in bipolar manic depressive psychosis. *Life Sciences,* **15**, 1739–1748.

——, Burckhardt, W. & Jefferson, J. W. (1976) Increased erythrocyte Na^+ pump and Na-K ATPase activity during lithium therapy. *Research Communications in Pathology and Pharmacology,* **14**, 117–126.

Johnston, B. B., Naylor, G. J., Dick, E. G., *et al* (1980) Prediction of the course of bipolar manic depressive illness treated with lithium. *Psychological Medicine,* **10**, 329–334.

Naylor, G. J. (1985) Reversal of vanadate-induced inhibition of Na^+,K^+-ATPase. A possible explanation of the therapeutic effect of carbamazepine in affective illness. *Journal of Affective Illness,* **8**, 329–334.

——, Dick, D. A. T., Dick, E. G., *et al* (1973) Erythrocyte membrane cation carrier in depressive illness. *Psychological Medicine,* **3**, 502–508.

——, ——, ——, *et al* (1974) Lithium therapy and erythrocyte membrane cation carrier. *Psychopharmacology*, **37**, 81–86.

——, ——, ——, *et al* (1976) Erythrocyte membrane cation carrier in mania. *Psychological Medicine*, **6**, 659–663.

—— & ——, Johnston, B. B., *et al* (1981) A possible explanation for the therapeutic action of lithium and a possible substitute (methylene blue). *Lancet*, *ii*, 1175–1176.

——, Smith, A. H. W., Boardman, L. J., *et al* (1977) Lithium and erythrocyte membrane cation carrier studies in normal and manic depressive subjects. *Pyschological Medicine*, **7**, 229–233.

——, ——, Dick, E. G., *et al* (1980) Erythrocyte membrane cation carrier in manic depressive psychosis. *Psychological Medicine*, **10**, 521–525.

—— & —— (1981) Vanadium; a possible aetiological factor in manic depressive illness. *Psychological Medicine*, **11**, 249–256.

——, ——, Bryce-Smith, D., *et al* (1984) Tissue vanadium levels in manic depressive psychosis. *Psychological Medicine*, **14**, 767–772.

——, Corrigan, F. M., Smith, A. H. W., *et al* (1987*a*) Further studies of vanadium in depressive psychosis. *British Journal of Psychiatry*, **150**, 656–661.

——, Smith, A. H. W. & Connelly, P. (1987*b*) A controlled trial of methylene blue in severe depressive illness. *Biological Psychiatry*, **22**, 657–659.

Nurnburger, J., Jimerson, D. C., Allen, J. R., *et al* (1982) Red cell ouabain-sensitive Na^+-K^+ adenosine triphosphatase: a state marker in affective illness inversely related to plasma cortisol. *Biological Psychiatry*, **17**, 981–991.

Pettegrew, J. W., Nichols, J. S., Minshew, N. J., *et al* (1982) Membrane biophysical studies of lymphocytes and erythrocytes in manic–depressive illness. *Journal of Affective Disorders*, **4**, 237–247.

Phillis, J. W. & Wu, P. H. (1981) Catecholamines and the sodium pump in excitable cells. *Progress in Neurobiology*, **17**, 141–184.

Sengupta, N., Datta, S. C., Sengupta, D., *et al* (1980) Platelet and erythrocyte membrane ATPase activity in depression and mania. *Psychiatry Research*, **3**, 337–344.

Thakar, J. H., Lapierre, Y. D. & Waters, B. G. (1985) Erythrocyte membrane sodium–potassium and magnesium ATPase affective disorder. *Biological Psychiatry*, **20**, 734–740.

Wood, A. J. (1987) Changes in cation transport during affective illness: do they have therapeutic implications? *Human Psychopharmacology*, **2**, 197–210.

—— & Goodwin, G. M. (1987) A review of the biochemical and neuropharmacological actions of lithium. *Psychological Medicine*, **17**, 579–600.

——, Viswalingam, A., Aronson, J. K., *et al* (1986) The effect of lithium on cation transport in vivo and in vitro in healthy volunteers. *British Journal of Clinical Pharmacology*, **21**, 609–610P.

——, Aronson, J. K., Cowen, P. J., *et al* (1987) In vivo measurement of cation transport in patients suffering from acute manic illness. *New Directions in Affective Illness*, p. 58. Proceedings of the International Conference, Jerusalem.

——, Brearley, C. J., Aronson, J. K., *et al* (1988*a*) The effect of salbutamol on in vivo cation transport. *British Journal of Clinical Pharmacology*, **25**, 624–625P.

——, Viswalingam, A., Glue, P., *et al* (1988*b*) Measurement of cation transport in vivo and in vitro in healthy volunteers after the oral administration of lithium carbonate. *Clinical Science*, (in press).

Young, R. C., Biggs, J. T., Ziegler, V., *et al* (1978) A rating scale for mania: reliability, validity and sensitivity. *British Journal of Psychiatry*, **153**, 429–435.

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Role of Modelling in In-Patient Suicide: a Lack of Supporting Evidence

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An analysis of the temporal distribution of 115 in-patient suicides that occurred in two Swiss psychiatric hospitals in the years 1977–86 failed to reveal any statistically significant clustering of suicides. Thus, the modelling effect does not generally play a decisive role in psychiatric in-patient suicide.

A family history of suicide increases the probability of a patient's suicidal behaviour (Roy, 1983). Among other factors, including a genetic one (Tsuang, 1977; Wender *et al*, 1986), the provision of a model has been claimed to be of importance (Farber, 1977). Suicidal behaviour, including completed suicide, is sometimes frequent in social groups of adolescent and young people (Kreitman *et al*, 1970; Ward & Fox, 1977; Robbins & Conroy, 1983; Ficker, 1987), even though suicidal patients do not always have more suicidal models than controls (Chiles *et al*, 1985). In recent times a possible modelling effect on suicidal behaviour (Werther effect) in larger populations has attracted attention, but the results seem to be equivocal: in some studies the number of suicides was found to increase after news or feature stories about true suicide in the newspapers and on television (Phillips, 1974; Bollen & Phillips, 1982; Phillips & Carstensen, 1986), but in other studies the effect of mass media on suicide rates could not be demonstrated (Horton & Stack, 1984; Stack, 1983; Littmann, 1985). The curtailing of newspaper reporting on suicides does not reduce the overall suicide rate, but seems to be followed by a reduction of suicides in young women (Motto, 1967, 1970; Blumenthal & Bergner, 1973). The broadcasting of a fictional television suicide story was found to increase the number of suicides (Schmidtke & Häfner, 1986; Gould & Shaffer, 1986), but the results could not be replicated (Phillips & Paight, 1987), and Platt (1987) failed to demonstrate a strong imitation effect on the frequency of suicidal behaviour of a televised fictional parasuicide.

Suicide occurs frequently in psychiatric hospitals, and the suicide rate among psychiatric in-patients considerably exceeds the suicide rate in the general population (Temoche *et al*, 1964; Modestin *et al*, 1985). Clinical suicides sometimes tend to occur in waves (Coser, 1976) or in epidemics (Jensen, 1966; Anonymous, 1977), and it has been speculated that the rumour of a suicide could activate latent suicidal tendencies in other patients (Jensen, 1966). Therefore, hospital staff should be aware of the influence of imitation in suicide (Zemishlany *et al*, 1987). To our knowledge, however, up to the present the role of suggestion and of imitation and modelling in suicide of psychiatric in-patients has not been investigated empirically in a systematic manner. Therefore, the present study was undertaken.

Method

All in-patients who had committed suicide were identified by examination of the police files (the most complete registration of suicides in Switzerland). Their suicide had occurred while they were on the hospital rolls of two Swiss psychiatric institutions in the years 1977–86. Both psychiatric hospitals provide primary in-patient care for all psychiatric patients of the area. Each of the two hospitals had 500–600 beds and was organised in units of about 20 beds. All suicides were included, irrespective of whether they were committed in the hospital itself, during short-term leave, or during an escape. The temporal distribution of the suicides was carefully registered separately for each of the two hospitals.

Statistical analysis

To investigate whether the suicides were uniformly distributed over the whole ten-year period, the observed suicide frequencies in each year were compared with the expected ones (the average number of suicides per year) with the help of the χ^2 test.

If a suicide really increases the probability of the occurrence of the next one, then shorter time periods between individual suicides should be observed more frequently than for random events. If suicide is an independent act, the distribution of the intervals between two suicides should follow the negative binominal distribution. This distribution indicates the probability of an event's occurring after a certain time period during which no event occurred. The corresponding formula is $P(x/p,\ k) = p(1-p)^k$, where $P(x/p,\ k)$ is the conditional probability of a suicide's (x) occurring on day $k+1$ after k days without suicide, and p is the probability of a suicide as an elementary event. The latter (p) is given by the reciprocal value of the average time interval between two suicides. In order to investigate whether there was a difference between the observed and theoretical distributions of the intervals between suicides, cumulative distributions were arranged and compared with the help of the Kolmogorov–Smirnov test.

Results

Sixty-one suicides were registered in the first psychiatric hospital, and 54 suicides in the second. The average number of suicides per year amounted to 6.1 in the first institution and 5.4 in the second. Comparison of the real and expected frequencies per year yielded χ^2 values of 11.62 and 10.07 (d.f. $= 9$), these values not being statistically significant. Thus, even though there was some fluctuation of the suicide frequency, the differences between individual years did not reach the level of statistical significance (probability < 0.05).

Comparing the observed and expected cumulative distributions of the intervals between suicides with the help of the Kolmogorov–Smirnov test, the maximal differences between the observed and expected distribution functions amounted to 0.082 for the first institution and 0.079 for the second. Neither value is statistically significant. The real intervals between two suicides corresponded almost exactly to the theoretically expected ones. Thus, in both institutions the distribution of suicides followed a random pattern. No indication was found of an increased probability of a suicide occurring soon after the previous suicide.

Discussion

In both institutions involved in the study, suicide occurred frequently in the course of the ten-year period investigated. The suicide rates for the institutions were as high as 358 and 334 per 100 000 in-patients treated. Correspondingly, Switzerland numbers among the countries with a high general suicide rate: 26 per 100 000 inhabitants in 1980. In our study, using statistical methods of evaluation, we failed to demonstrate a significant temporal clustering effect of suicide in the first psychiatric institution and we were able to validate this finding in the other. In contrast to this result, Niemi (1975), applying a similar method of study to Finnish gaols during 1963–70, found a greater number of suicides committed within two days of the previous suicide than was expected. As no time–space clustering could be verified in that study, the interpretation of his result is difficult. Regarding our negative finding, we conclude that, in psychiatric in-patient suicide, suggestion and imitative modelling or identification do not play a decisive role. Several factors might be of importance regarding this result.

Contagion effects were claimed to be less pronounced in psychotic than in other patients (Häfner *et al*, 1983), and a large proportion of our in-patients are indeed psychotics. Also, the imitative influence of suicidal behaviour plays a role primarily in adolescents (Schmidtke & Häfner, 1986; Phillips & Carstensen, 1986; Ficker, 1987). This age group is hardly represented among our in-patients, and this fact may account for a great deal of the difference between our negative findings regarding the Werther effect and some positive ones found in other populations.

It is improbable that the absence of susceptible, suicide-prone individuals could account for our result. At every point of time there were suicidal, depressed patients as well as socially handicapped, severely ill schizophrenic patients in both hospitals. Precisely these two groups have been shown to be particularly prone to suicide (Modestin, 1986). Severely ill in-patients might be too autistic or too preoccupied by their own problems to take notice of the suicide of a fellow patient. The everyday observations are at variance with this assumption, however. Generally the fellow patients of the same unit do register such events, and besides, there are relatively close social networks in both institutions, increasing the likelihood of the 'contagion' effect: the patients of different units work together in the central workshops and they meet in the central social facilities. Also, following suicide, the staff inform the fellow patients and invite them to talk about it. After every suicide the staff doubtless observe the patients more carefully, caring more intensively for those who might be increasingly at risk. The possible effect of suggestion could be so successfully countered by these measures as not to become manifest. On the other hand, following the suicide of a patient, the staff regularly tend to be less emotionally stable and less professionally self-confident for some time. Should the staff indeed be that successful in preventing further fatalities following a suicide in spite of their destabilisation, it would be difficult to explain the high incidence of suicide at other times. It is improbable that the quality of care fluctuates to any great extent.

Thus, we rather think that the probability of a suicide is not much higher following another suicide than at other times, and that the influence of suggestion does indeed not play a substantial role regarding suicide. Whereas our findings concern completed suicide, they may not apply to non-fatal suicidal acts. Clusters of self-mutilation episodes in adolescent units have been described (Offer & Barglow, 1960; Matthews, 1968) and the finding has been statistically substantiated (Walsh & Rosen, 1985). Could the non-inclusion of the non-fatal suicidal acts in our study have influenced the result? Patients committing and attempting suicide behave differently, belonging to different, though overlapping populations (Stengl, 1973). The population of self-mutilators differs from other suicide attemptors in terms of motivation and the lethality of the act (Grunebaum & Klerman, 1967; Simpson, 1976). Correspondingly, acts of completed suicide were not observed during the epidemics of self-mutilatory behaviour (Offer & Barglow, 1960; Matthews, 1968; Simpson, 1975; Kroll, 1978; Walsh & Rosen, 1985). Thus, we do not believe that the non-inclusion of non-fatal suicidal acts biased our result. However, as we cannot exclude this possibility entirely, both types of behaviour might be considered in future studies.

Our negative result does not preclude the possibility of modelling's playing a role in individual cases of clinical suicide, as described, for instance, by Crawford & Willis (1966). According to Durckheim (1897), imitation may play an important role in an individual suicide although it does not influence the general suicide rate. Observation of epidemics of completed suicide in psychiatric hospitals seems to have been carried out mainly in those psychiatric hospitals where suicide is a much rarer phenomenon. Our results suggest that even those 'epidemics' do not necessarily occur because of the effect of modelling, but that the occurrence of multiple suicides may have a different common cause. Indeed, micro-social influences such as organisational instability, lowered staff morale, weakening of the relational system of the staff, and shortcomings in leadership have all been identified as being of importance at the time of such epidemics (Kahne, 1968; Coser, 1976; Anonymous, 1977; Langley & Bayatti, 1984).

References

Anonymous (1977) A suicide epidemic in a psychiatric hospital. *Diseases of the Nervous System*, **38**, 327–331.

Blumenthal, S. & Bergner, L. (1973) Suicide and newspapers: a replicated study. *American Journal of Psychiatry*, **130**, 468–471.

Bollen, K. A. & Phillips, D. P. (1982) Imitative suicides: a national study of the effects of television news stories. *American Sociological Review*, **47**, 802–809.

Chiles, J. A., Strosahl, K. D., McCurtray, L., *et al* (1985) Modeling effects on suicidal behavior. *Journal of Nervous and Mental Disease*, **173**, 477–481.

Coser, R. L. (1976) Suicide and the relational system: a case study in a mental hospital. *Journal of Health and Social Behavior*, **17**, 318–327.

Crawford, J. P. & Willis, J. H. (1966) Double suicide in psychiatric hospital patients. *British Journal of Psychiatry*, **112**, 1231–1235.

Durckheim, E. (1897) *Suicide*. New York: Free Press (1957).

Farber, M. L. (1977) Factors determining the incidence of suicide within families. *Suicide & Life-Threatening Behavior*, **7**, 3–6.

Ficker, F. (1987) Vorbildwirkung für suizidales Handeln junger Menschen. *Pädiatrie und Grenzgebiete*, **26**, 391–395.

Gould, M. S. & Shaffer, D. (1986) The impact of suicide in television movies: evidence of imitation. *New England Journal of Medicine*, **315**, 690–694.

Grunebaum, H. U. & Klerman, G. L. (1967) Wrist slashing. *American Journal of Psychiatry*, **124**, 527–534.

Häfner, H., Welz, R., Gorenc, K., *et al* (1983) Selbstmordversuche und depressive Störungen. *Schweizer Archiv für Neurologie, Neurochirurgie und Psychiatrie*, **133**, 283–294.

Horton, H. & Stack, S. (1984) The effect of television on national suicide rates. *Journal of Social Psychology*, **123**, 141–142.

Jensen, L. (1966) Nosocomial suicides and suicides among discharged patients. *Acta Psychiatrica Scandinavica*, **42** (suppl. 191), 149–170.

Kahne, M. J. (1968) Suicides in mental hospitals: a study of the effects of personnel and patient turnover. *Journal of Health and Social Behavior*, **9**, 255–266.

Kreitman, N., Smith, P. & Eng-Seong, T. (1970) Attempted suicide as language: an empirical study. *British Journal of Psychiatry*, **116**, 465–473.

Kroll, J. L. (1978) Self-destructive behavior on an inpatient ward. *Journal of Nervous and Mental Disease*, **166**, 429–434.

Langley, G. E. & Bayatti, N. N. (1984) Suicides in Exe Vale hospital, 1972–1981. *British Journal of Psychiatry*, **145**, 463–467.

Littmann, S. K. (1985) Suicide epidemics and newspaper reporting. *Suicide & Life Threatening Behavior*, **15**, 43–50.

Matthews, P. C. (1968) Epidemic self-injury in an adolescent unit. *International Journal of Social Psychiatry*, **14**, 125–133.

Modestin, J. (1986) Three different types of clinical suicide. *European Archives of Psychiatry and Neurological Sciences*, **236**, 148–153.

——, Brenner, H. & Koch, U. (1985) To the problem of an institutional suicide. In *Psychiatry: the State of the Art* (eds P. Pichot, P. Berner, R. Wolf & K. Thau), pp. 939–944. New York, London: Plenum Press.

Motto, J. A. (1967) Suicide and suggestibility – the role of the press. *American Journal of Psychiatry*, **124**, 252–256.

—— (1970) Newspaper influence on suicide: a controlled study. *Archives of General Psychiatry*, **23**, 143–148.

Niemi, T. (1975) The time-space distances of suicides committed in the lock-up in Finland in 1963–1967. *Psychiatria Fennica*, **6**, 267–270.

Offer, D. & Barglow, P. (1960) Adolescent and young adult self-mutilation incidents in a general psychiatric hospital. *Archives of General Psychiatry*, **3**, 194–204.

Phillips, D. P. (1974) The influence of suggestion on suicide: substantive and theoretical implications of the Werther effect. *American Sociological Review*, **39**, 340–354.

—— & Carstensen, L. L. (1986) Clustering of teenage suicides after television news stories about suicide. *New England Journal of Medicine*, **315**, 685–689.

—— & Paight, D. J. (1987) The impact of televised movies about suicide: a replicative study. *New England Journal of Medicine*, **317**, 809–811.

Platt, S. (1987) The aftermath of Angie's overdose: is soap (opera) damaging to your health? *British Medical Journal*, **294**, 954–957.

Robbins, D. & Conroy, R. C. (1983) A cluster of adolescent suicide attempts: is suicide contagious? *Journal of Adolescent Health Care*, **3**, 253–255.

Roy, A. (1983) Family history of suicide. *Archives of General Pychiatry*, **40**, 971–974.

Schmidtke, A. & Häfner, H. (1986) Die Vermittlung von Selbstmordmotivation und Selbstmordhandlung durch fiktive Modelle. *Nervenarzt*, **57**, 502–510.

Simpson, M. A. (1975) The phenomenology of self-mutilation in a general hospital setting. *Canadian Psychiatric Association Journal*, **20**, 429–434.

—— (1976) Self-mutilation and suicide. In *Suicidology: Contemporary Developments* (ed. E. S. Shneidman), pp. 281–315. New York: Grune & Stratton.

STACK, S. (1983) The effect of the Jonestown suicides on American suicide rates. *Journal of Social Psychology*, **119**, 145–146.

STENGEL, E. (1973) *Suicide and Attempted Suicide*. Harmondsworth: Penguin Books.

TEMOCHE, A., PUGH, T. F. & MACMAHON, B. (1964) Suicide rates among current and former mental institution patients. *Journal of Nervous and Mental Disease*, **138**, 124–130.

TSUANG, M. T. (1977) Genetic factors in suicide. *Diseases of the Nervous System*, **38**, 498–501.

WALSH, B. W. & ROSEN, P. (1985) Self-mutilation and contagion: an empirical test. *American Journal of Psychiatry*, **142**, 119–120.

WARD, J. A. & FOX, J. (1977) A suicide epidemic on an Indian reserve. *Canadian Psychiatric Association Journal*, **22**, 423–426.

WENDER, P. H., KETY, S. S., ROSENTHAL, D., *et al* (1986) Psychiatric disorders in the biological and adoptive families of adopted individuals with affective disorders. *Archives of General Psychiatry*, **43**, 923–929.

ZEMISHLANY, Z., WEINBERGER, A., BEN-BASSAT, M., *et al* (1987) An epidemic of suicide attempts by burning in a psychiatric hospital. *British Journal of Psychiatry*, **150**, 704–706.

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Abnormal Eating Attitudes in Young Insulin-Dependent Diabetics

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All insulin-dependent diabetics between the ages of 16 and 25 years attending the diabetic clinic at the Royal Infirmary, Edinburgh, (152 women and 139 men) were asked to complete the EAT, the EDI, and the GHQ, and to provide a control subject (sibling or close friend) of similar age who would do likewise. Marked differences were found between diabetic women (but not men) and their controls in eating attitudes, in many of the psychological characteristics associated with eating disorders, and in GHQ scores. Although some of the women had classic anorexia nervosa or bulimia, others with abnormal eating attitudes did not fulfil the formal criteria. Overall, diabetics were significantly heavier than controls but the differences in eating attitudes were not eliminated by correcting for overweight. Abnormal scores were associated with high HbA_1 levels and independently with retinopathy. The weight gain and psychological effects of diabetes are identified as probably of aetiological importance in the abnormal eating attitudes of young diabetic women.

The co-existence of anorexia nervosa and diabetes was first reported from our clinic (Fairburn & Steel, 1980). Since then, several reports have stressed the difficulties of treating both conditions simultaneously (Gomez *et al*, 1980; Roland & Bhanji, 1982; Powers *et al*, 1983; Malone & Armstrong, 1985). The syndrome of bulimia nervosa was first described in 1979 (Russell, 1979) and its association with diabetes has also been reported (Hillard *et al*, 1983; J. I. Hudson *et al*, 1983; Hudson, M. S. *et al*, 1983; Szmukler, 1984; Hillard & Hillard, 1984; Nielsen *et al*, 1987). We have recorded a high prevalence of clinically apparent eating disorders in a survey of young insulin-dependent diabetic women (Steel *et al*, 1987).

The present study, using previously validated questionnaires, has assessed the prevalence of abnormal attitudes to eating, which characteristically occur in anorectic or bulimic patients, in a large cohort of insulin-dependent diabetics and matched non-diabetic controls. We have also examined possible associations between abnormal attitudes to eating, weight, glycaemic control, and complications of diabetes suggested by our previous study (Steel *et al*, 1987).

Method

All insulin-dependent diabetics between the ages of 16 and 25 years in 1985 who had attended the diabetic clinic at the Royal Infirmary, Edinburgh, during the previous year were included in the study with the exception of five (two who were mentally retarded and three who had another serious medical illness). There were 152 women and 139 men. Each patient was asked to provide a non-diabetic control: a sibling of the same sex, or if a suitable sibling was not available, a friend of the same sex and similar age. This method of selecting controls was chosen in an attempt to minimise differences between the control and diabetic groups in genetic, psychological, and sociocultural factors, which are all thought to influence susceptibility to eating disorders (Rosmark *et al*, 1986).

The study consisted of a postal survey backed up, in the case of the diabetics, by personal contact during attendance at the clinic. Patients and controls were asked to complete a questionnaire covering demographic data, the Eating Attitude Test (EAT–40; Garner & Garfinkel, 1979), the Eating Disorder Inventory (EDI; Garner *et al*, 1983) and the 30-item version of the General Health Questionnaire (GHQ; Goldberg, 1972). The EAT–40 has been used as a screening instrument for detecting cases of anorexia nervosa in groups at high risk for this disorder, and for identifying abnormal eating patterns, for example among college students (Garner & Garfinkel, 1980). It consists of 40 questions describing attitudes or behaviour. The questions are grouped into three subscales: dietary, bulimia, and oral control. The EDI is a multifaceted instrument designed to assess psychological characteristics relevant to anorexia nervosa and bulimia. It consists of 64 questions divided into eight subscales: drive for thinness, body dissatisfaction, maturity fears, bulimia, interoceptive awareness, perfectionism, ineffectiveness, and interpersonal distrust. The GHQ has been shown to be a reliable screening test for psychiatric illness, and has been used in several studies in various medical settings (Goldberg & Blackwell, 1970; Bridges & Goldberg, 1986). Because it is recognised that diabetes *per se* can influence certain aspects of eating attitudes, ten members of the medical staff working in the diabetic clinic were asked to complete the EAT and EDI as though they were "sensible young diabetics without an eating disorder", so as to identify any questions to which respondents might give biased answers simply by following recommended diabetic treatment guidelines. A question was considered to be biased if over half the medical staff independently suggested it to be so.

As an indicator of diabetic control, glycosylated haemoglobin (HbA_1) was measured in diabetic patients at the time of the study, and fundi were examined for retinopathy. Patients with high scores on the EAT were interviewed.

Statistical analysis

Data from diabetic patients and matched controls were compared using a paired *t*-test. Comparisons were made before and after the removal of items which were thought to be affected by diabetes (adjusted score). Question 23 on EAT relating to menstruation was excluded from the analysis of the men. Median values were used to illustrate the level of each variable in the four groups, because the distribution of the scores was markedly skewed. Patients with and without a matched control were compared to ensure that exclusion of those without a control did not affect the analysis.

As the diabetics were significantly heavier than the controls, the results were re-analysed with correction for body mass index (BMI) by analysis of covariance. Spearman rank correlation coefficients were calculated between BMI and adjusted scores.

The relationship between adjusted scores and diabetic control was investigated by use of multiple linear regression, with HbA$_1$ as the dependent variable; sex, age and GHQ were forced into the regression and the eating scores were included as other explanatory variables.

The relationship between retinopathy and eating scores was investigated by use of logistic regression. Diabetic patients were divided into those with and without retinopathy, and the odds of having retinopathy were related to the eating scores. Duration of diabetes and HbA$_1$ were forced into the regression as explanatory variables.

In both regression models the square root of the eating score was used, to moderate the influence of the occasional high value on the models.

TABLE I
Median values for basic data and scores of diabetics and controls

	Women		*Men*	
	Diabetic (n = 147)	*Control (n = 138)*	*Diabetic (n = 126)*	*Control (n = 73)*
Age: years	22.0	21.0	22.0	21.0
Height: m	1.63	1.63	1.78	1.78
Weight: kg	60.4	57.2	72.8	68.5
BMI: kg/m^2	23.2	21.6	23.2	21.8
HbA$_1$: %	11.0	–	10.0	–
Duration of diabetes: years	11.0	–	9.0	–
Age of onset: years	11.0	–	12.0	–
EAT Total	15.4	8.0	10.3	6.2
Total – adjusted score[1]	9.4	6.0	5.3	4.1
Diet	0.54	0.15	0.31	0.08
Diet – adjusted score[1]	0.25	0.0	0.0	0.0
Bulimia	0.0	0.0	0.0	0.0
Oral control	0.29	0.14	0.29	0.29
Oral control – adjusted score[1]	0.0	0.0	0.0	0.0
EDI subscores				
Drive for thinness	0.57	0.29	0.14	0.0
Drive for thinness – adjusted score[1]	0.25	0.0	0.0	0.0
Body dissatisfaction	1.7	1.0	0.44	0.33
Maturity fears	0.25	0.13	0.13	0.25
Bulimia	0.0	0.0	0.0	0.0
Interoceptive awareness	0.10	0.10	0.0	0.10
Perfectionism	0.33	0.33	0.67	0.67
Ineffectiveness	0.20	0.10	0.10	0.0
Interpersonal distrust	0.43	0.29	0.43	0.43
GHQ	4.0	1.0	1.0	1.0

1. Values when diabetes-biased questions omitted.

TABLE II
Summary of comparisons between diabetics and paired controls

	Women (138 pairs)		*Men (73 pairs)*	
	Mean difference	*95% confidence interval*	*Mean difference*	*95% confidence interval*
EAT Total	8.91	6.6,11.3***	3.71	1.8,5.6***
Total - adjusted score[1]	5.43	3.35,7.52	1.06	−0.32,2.44
Diet	0.43	0.33,0.52***	0.20	0.12,0.29***
Diet - adjusted score[1]	0.28	0.16,0.41***	0.03	−0.05,0.10
Bulimia	0.14	0.05,0.23**	0.02	−0.06,0.09
Oral control	0.09	0.01,0.17*	−0.04	−0.13,0.04
Oral control - adjusted score[1]	0.06	−0.02,0.14	−0.09	−0.16, −0.01
EDI subscores				
Drive for thinness	0.44	0.28,0.61***	0.13	0.02,0.25*
Drive for thinness - adjusted score[1]	0.41	0.22,0.60***	0.05	−0.08,0.17
Body dissatisfaction	0.48	0.26,0.70***	0.04	−0.10,0.19
Maturity fears	0.02	−0.05,0.10	−0.04	−0.14,0.06
Bulimia	0.03	−0.05,0.11	−0.03	−0.10,0.04
Interoceptive awareness	0.09	0.01,0.17*	0.02	−0.05,0.09
Perfectionism	0.03	−0.10,0.16	−0.03	−0.23,0.18
Ineffectiveness	0.14	0.05,0.24**	0.12	0.02,0.23*
Interpersonal distrust	0.11	0.02,0.21*	0.09	−0.07,0.25
GHQ	1.58	0.09,3.07*	0.52	−1.22,2.26

1. Values when diabetes-biased questions omitted.
*$P<0.05$; ** $P<0.01$; *** $P<0.001$.

Results

Of the 152 diabetic women, 147 (97%) completed the questionnaires, four failed to fill them in, and one refused; 138 provided suitable controls. Of the 139 diabetic men, 126 (91%) completed the questionnaires, eleven failed to do so, and two refused; 73 provided suitable controls. Basic data for diabetics and controls are shown in Table I. There were no significant differences with regard to age or height, but diabetics were significantly heavier than their controls (women, $P<0.001$; men, $P<0.05$).

Comparisons of EAT, EDI and GHQ scores are summarised in Tables I and II. There were 51 men who did not have controls, but comparison of median scores in those with and without controls showed no difference between the two groups.

Before the removal of diabetes-biased questions, the diabetic women obtained significantly higher scores than their controls in the total EAT and all the EAT subscales, and in the EDI subscales drive for thinness, body dissatisfaction, interoceptive awareness, ineffectiveness and interpersonal distrust. The GHQ score was also significantly higher for the diabetic women. By contrast, for the men there were much smaller differences between diabetics and controls: they were significant only for total EAT, EAT subscale diet, and EDI subscale drive for thinness and ineffectiveness.

The questions determined to be biased by diabetes are listed in Table III. The data were re-analysed after removal of these questions. The adjusted scores are included in Tables I and II. In women, all differences between diabetics and controls remained significant except on the oral control subscale of the EAT. By contrast, in men, differences between diabetics and controls for all the scores became insignificant, except on the ineffectiveness subscale of the EDI. A score of above 30 (90th centile) on EAT is thought to identify probable clinical abnormality (Garner & Garfinkel, 1979). After elimination of some questions, the distribution in normals is obviously changed. The 90th centile for control women after elimination of the diabetes-biased questions was 18. Two (3%) control men, five (4%) diabetic men and 30 (20%) diabetic women had scores of more than 18. There were 12 diabetics who were known to have a clinical eating disorder and 4 known to have a partial syndrome. Fourteen of these 16 scored above 18; the other two had very low scores and clearly had not

TABLE III
Questions removed in adjusted scores
EAT

Scale and number	*Question*	*Subscale*
EAT		
9	Aware of calorie content of foods eaten	Diet
29	Avoid foods with sugar in them	Diet
30	Eat diet foods	Diet
32	Display self-control around food	Oral control
36	Feel comfortable about eating sweets	Diet
39	Enjoy trying new rich foods	Diet
EDI		
1	I eat sweets and carbohydrate without feeling nervous	Drive for thinness
7	I think about dieting	Drive for thinness
11	I feel extremely guilty after overeating	Drive for thinness

answered the questions honestly. The other 21 high-scoring diabetic patients were interviewed, and all had a preoccupation with food, body image and shape.

The mean difference in GHQ scores between diabetic women and controls was 1.58 ($P<0.05$), but there was no significant difference between diabetic men and controls. The threshold GHQ score of 4/5 for identifying cases in a community sample has been found to have low specificity in a medical population (Feldman *et al*, 1987) so we adopted a higher threshold of 11/12, this being the best cut-off on the 28-item GHQ when used in neurological patients (Bridges & Goldberg, 1984). Using this cut-off, scores indicating probable psychiatric morbidity were obtained by 32 (22%) diabetic women, 22 (16%) control women, 11 (9%) diabetic men and 4 (6%) control men.

EAT was correlated with GHQ: diabetic men $r=0.21$, $p<0.05$; control men, $r=0.14$, NS; diabetic women, $r=0.38$, $p<0.001$; control women, $r=0.45$, $p<0.001$.

After correction for BMI, there remained an appreciable difference between diabetic women and controls for total EAT ($P<0.001$), and a slight difference for drive for thinness ($P<0.05$). The Spearman correlation coefficient between BMI and scores showed significant relationships ($P<0.005$) only for total EAT in diabetic women ($r=0.23$), for the EAT subscore diet for diabetic women ($r=0.33$) and control women ($r=0.28$), for the EDI subscore drive for thinness in diabetic women ($r=0.33$) and control women ($r=0.32$), and the EDI subscore body dissatisfaction in all subjects (diabetic women, $r=0.59$; control women, $r=0.83$; diabetic men, $r=0.40$; control men, $r=0.39$). The relationships for diabetic women between BMI and total EAT, body dissatisfaction and drive for thinness are shown in Fig. 1.

The partial correlations of HbA_1 with total EAT, EAT subscores and EDI subscores were determined. HbA_1 was significantly correlated with total EAT ($r=0.25$, $P<0.001$) and its diet and oral control subscores ($r=0.14$, $P<0.05$, $r=0.26$, $P<0.001$, respectively), and less so with EDI subscores (for bulimia and interoceptive awareness, $r=0.15$, $P<0.05$).

Retinopathy was found in 53 diabetic patients. After allowing for duration of diabetes and HbA_1 in the logistic regression model, there were significant associations between the presence of retinopathy and total EAT ($P<0.01$), EAT subscores bulimia and diet ($P<0.05$), EDI subscores bulimia and interoceptive awareness ($P<0.05$), and GHQ ($P<0.05$). An estimate of the odds ratio of retinopathy occurring in subjects who had abnormal EAT (more than 18) as compared with subjects who had normal EAT is 2.5, with 95% confidence interval 1.04–6.1.

Discussion

In our previous survey of 208 insulin-dependent diabetic women between the ages of 16 and 25 years, we found that 15 (7%) had a clinically apparent eating disorder (Steel *et al*, 1987). That study was thought to underestimate the prevalence of eating disorders, particularly of bulimia, since only clinically obvious cases were included, and detailed questionnaires were not used.

In order to obtain a more accurate estimate of the size of the problem and to look at attitudes to eating in more detail, it is appropriate to use standardised questionnaires, and some studies of this type have already been published. Wing *et al* (1986) found higher scores in diabetics using the EAT, but their results are difficult to interpret as they did not remove diabetes-related questions. Rodin *et al* (1985) used the EAT and EDI in a sample of 46 female diabetics. They again did not correct for diabetes-related

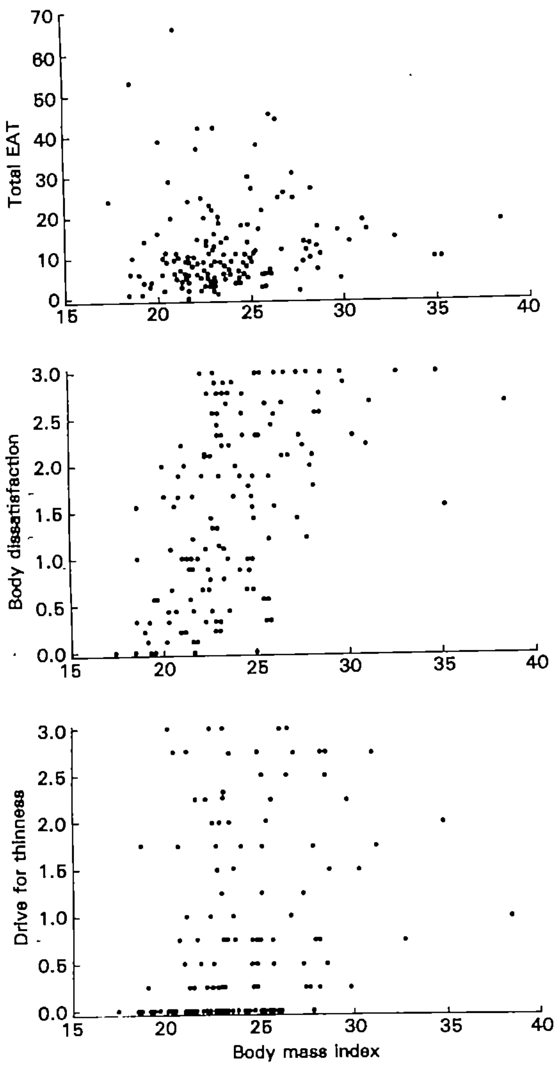

FIG. 1 Relationships for diabetic women between BMI and total EAT, body dissatisfaction and drive for thinness.

questions, but did show that 9 out of 19 patients with high scores suffered from anorexia or bulimia or a partial syndrome. Rosmark *et al* (1986) removed diabetes-related questions and found that as a group their 41 female diabetics had higher mean scores on the EAT than two comparison groups, one composed of female controls and the other of male diabetics. Our present study is much larger than those previously reported; it is the first to include the EDI after removing diabetes-related questions and the first to examine the relationship between these scores, body mass index (BMI) and retinopathy.

Our results show higher EAT and EDI scores in diabetic women than in their controls. These differences are likely to reflect a genuinely higher prevalence of eating disorders in diabetic women, as the differences remained highly significant after the removal of questions where answers might be influenced by diabetes *per se*. By contrast, removal of these questions eliminated almost all the differences between male diabetics and their controls. We still consider that our findings may underestimate the problem: whereas all those patients recording high scores, even those who could not be formally classified as having anorexia nervosa or bulimia, did appear to be obsessed by food and by their body weight and image, two of our patients known to have eating disorders clearly filled in the questionnaire dishonestly. Furthermore, in relation to bulimia, we know that rather than vomiting many of our female diabetics reduce their dose of insulin to achieve a similar calorie-voiding effect (Steel, 1987, 1989). Thus eating disorder appears to be a feature predominantly of the female population, the high prevalence in diabetics reflecting their greater vulnerability to the same processes that may lead to expression of an eating disorder in non-diabetic women.

There is a tendency shown in this study for diabetics to be slightly more overweight than controls specifically selected from similar sociocultural backgrounds. This may be partly because insulin delivered systemically rather than into the portal circulation relatively overstimulates adipose tissue formation, and partly because many patients exceed their dietary allowance but are reluctant to eat less because of the risk of hypoglycaemia. Our interviews with diabetics who scored high suggested that this tendency to be overweight, and particularly the rapid weight gain following diagnosis, may be aetiologically important in the development of their eating disorders. Following diagnosis and the start of treatment, diabetics often regain weight rapidly owing to a combination of rehydration and the anabolic effect of insulin. Many described the experience as 'alarming', and several developed an eating disorder shortly after this had happened. That sequence of events occurred not only in those who had become overweight but also in those who changed from being overweight to being of average weight. Although weight appears to be important, the higher scores of the diabetic women cannot be attributed solely to this. It is true that some of the differences are reduced when the scores are adjusted for BMI, but EAT scores remain very significantly higher in diabetic women despite correction for BMI. Furthermore, it is clearly apparent from Fig. 1 that there are underweight, normal-weight and overweight subjects with high scores. Body dissatisfaction is really the only variable to show a close relationship with BMI (as might be expected). Our data therefore indicate that there must be other factors relating to diabetes which increase susceptibility to eating disorders.

Diabetics are constantly educated to focus on diet and food in order to control their diabetes, and are frequently made to feel guilty if they 'cheat'. It seems likely that this is aetiologically important. The high scores of interoceptive awareness, feelings of ineffectiveness, and interpersonal distrust reflect problems which are commonly encountered when one talks to young diabetic women. Higher GHQ scores in diabetic women than in control women and diabetic men have been described previously (Wilkinson *et al*, 1987), and neurotic symptoms tend to be associated with eating disorders. These results confirm the psychological impact of diabetes on young women and suggest that this probably increases the vulnerability of diabetic women to eating disorders. Our high-scoring patients found it helpful to be able to discuss their problem and to appreciate that they were not alone with their difficulties, but controlled studies are clearly needed to establish whether psychological intervention can reduce this morbidity.

Many observers have noted that eating disorders tend to be associated with poor diabetic control (Hillard & Hillard, 1984; Rodin *et al*, 1986). This study confirms the association. While some of our patients reduced their insulin in order to lose weight, others were found to be equally poorly controlled before and after the development of their disorder (Steel *et al*, 1987). The latter group may represent those who tend to cope badly with any problem. A further minority manage, with great effort, to control their diabetes relatively well during their eating disorder (Fairburn & Steel, 1980).

The significant association between some measures of abnormal eating attitudes and retinopathy, even after allowance for duration of diabetes, and HbA_1 (albeit a somewhat short-term measure of glycaemia), are in keeping with our previous observation (Steel *et al*, 1987) that early onset of severe diabetic complications is common in young diabetic women with eating disorders. The mechanism of this association is obscure. We have previously speculated that nutritional disturbance may provide the link. However, the association seems to hold even in diabetics of normal weight but with abnormal eating attitudes. Prospective studies are clearly required to shed more light on this difficult area.

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References

Bridges, K. & Goldberg, D. (1984) Psychiatric illness in patients with neurological disorders. *British Medical Journal*, **288**, 268–271.

—— & —— (1986) The validation of the GHQ 28 and the use of the MMSE in neurological in-patients. *British Journal of Psychiatry*, **148**, 548–553.

Fairburn, C. G. & Steel, J. M. (1980) Anorexia nervosa in diabetes mellitus. *British Medical Journal*, **280**, 1167–1168.

Feldman, E., Mayou, R., Hawton, K., *et al* (1987) Psychiatric disorders in medical in-patients. *Quarterly Journal of Medicine*, **63**, 405–417.

Garner, D. M. & Garfinkel, P. E. (1979) The eating attitudes test: an index of the symptoms of anorexia nervosa. *Psychological Medicine*, 9, 273–279.

—— & —— (1980) Socio-cultural factors in the development of anorexia nervosa. *Psychological Medicine*, **10**, 647–656.

——, Olmsted, M. P. & Polivy, J. (1983) Development and validation of a multi-dimensional eating disorder inventory for anorexia nervosa and bulimia. *International Journal of Eating Disorders*, **2**, 15–34.

Goldberg, D. P. (1972) *The Detection of Psychiatric Illness by Questionnaire*, Maudsley Monograph No. 21. Oxford: Oxford University Press.

—— & Blackwell, B. (1970) Psychiatric illness in general practice: detailed study using a new method of case identification. *British Medical Journal*, *ii*, 439–443.

Gomez, J., Dally, P. & Isaacs, A. J. (1980) Anorexia in diabetes mellitus. *British Medical Journal*, *ii*, 61–62.

Hillard, J. R., Lobo, M. C. & Keeling, R. P. (1983) Bulimia and diabetes: a potentially life threatening combination. *Psychosomatics*, **24**, 292–295.

—— & Hillard, P. J. A. (1984) Bulimia, anorexia nervosa and diabetes: deadly combinations. *Psychiatric Clinics of North America*, **7**, 367–379.

Hudson, J. I., Hudson, M. S. & Wentworth, S. M. (1983*a*) Self-induced glycosuria: a novel method of purging in bulimia. *Journal of the American Medical Association*, **249**, 2501.

—— M. S., Wentworth, S. M. & Hudson, J. I. (1983*b*) Bulimia and diabetes. *New England Journal of Medicine*, **309**, 431–432.

Malone, G. L. & Armstrong, B. K. (1985) Treatment of anorexia nervosa in a young adult patient with diabetes mellitus. *Journal of Nervous and Mental Disease*, **173**, 509–511.

Nielsen, S., Borner, H. & Kabel, M. (1987) Anorexia nervosa/bulimia in diabetes mellitus. *Acta Psychiatrica Scandinavica*, **75**, 464–473.

Powers, P. S., Malone, J. I. & Duncan, J. A. (1983) Anorexia nervosa and diabetes mellitus. *Journal of Clinical Psychiatry*, **44**, 133–135.

Rodin, G. M., Daneman, D., Johnson, L. E., *et al* (1985) Anorexia nervosa and bulimia in female adolescents with insulin-dependent diabetes mellitus: a systematic study. *Journal of Psychiatric Research*, **19**, 381–384.

——, Johnson, L. E., Daneman, D., *et al* (1986) Eating disorders in female adolescents with insulin dependent diabetes mellitus. *International Journal of Psychiatry in Medicine*, **16**, 49–57.

Roland, J. M. & Bhanji, S. (1982) Anorexia nervosa occurring in patients with diabetes mellitus. *Postgraduate Medical Journal*, **58**, 354–356.

ROSMARK, B., BERNE, C., HOLMGREN, S., *et al* (1986) Eating disorders in patients with insulin-dependent diabetes mellitus. *Journal of Clinical Psychiatry*, 47, 547–550.

RUSSELL, G. M. (1979) Bulimia nervosa – an ominous variant of anorexia nervosa. *Psychological Medicine*, 9, 429–448.

STEEL, J. M. (1987) Eating disorders and diabetes. *Practical Diabetes*, 4, 256.

—— (1989) Eating disorders and diabetes. In *Textbook of Diabetes* (eds J. Pickup & G. Williams). Oxford: Blackwell Scientific Publications (in press).

——, YOUNG, R. J., LLOYD, G. G., *et al* (1987) Clinically apparent eating disorders in young diabetic women: associations with painful neuropathy and other complications. *British Medical Journal*, 294, 859–862.

SZMUKLER, G. I. (1984) Anorexia and bulimia in diabetics. *Journal of Psychosomatic Research*, 28, 365–369.

WILKINSON, G., BORSEY, D. Q., LESLIE, P., *et al* (1987) Psychiatric disorder in patients with insulin-dependent diabetes mellitus attending a general hospital clinic: i) two stages screening and ii) detection by physicians. *Psychological Medicine*, 17, 515–517.

WING, R. A., NOWALK, M. P., MARCUS, M. D., *et al* (1986) Subclinical eating disorders and glycaemic control in adolescents with Type I diabetes. *Diabetes Care*, 9, 162–167.

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Clinical and Therapeutic Monitoring of Epilepsy in a Mental Handicap Unit

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Within a group of hospitals for the mentally handicapped serving the Leicestershire district, a cohort of 215 epileptic patients was identified, who were followed up for four years. The anticonvulsant medication of each patient was reviewed regularly until an optimal balance between seizure control, absence of medication side-effects, and reduction of polypharmacy was attained. After four years 172 patients remained in the study. A significant reduction in polypharmacy was attained overall. Some groups of patients showed a significant reduction in the frequency of seizures, while a small group of patients with frequent seizures remained difficult to control.

Epilepsy is a common problem of mentally handicapped patients. Corbett *et al* (1975) studied the prevalence of epilepsy in all the known severely mentally handicapped children in a London suburb with a population of about 175 000. They showed that of children with severe mental handicap (IQ under 50) a third had a history of seizures, and 19% had had at least one fit during the previous year. Similar findings were made by Tizard & Grad (1961). Additionally, Corbett (1981) showed that the prevalence of epilepsy increased in association with the severity of the mental handicap.

Mentally handicapped patients are also particularly vulnerable to the side-effects of medication, since they may be unable to conceptualise their experiences, or to communicate their experiences to their carers adequately. It is generally believed that the use of most of the anticonvulsants, possibly with the exceptions of carbamazepine and sodium valproate (Dodrill & Troupin, 1977; Thompson *et al*, 1981; Thompson & Trimble, 1982; Hirtz & Nelson, 1985) lead to cognitive impairments. While it is recognised that unwanted side-effects occur when the serum concentration of the drug lies within the toxic range, such effects in particular cognitive impairment, may also occur within the therapeutic range. Phenobarbitone has been shown to have adverse behavioural effects in children (Reynolds & Travers, 1974; Reynolds, 1975; Stores, 1975; Trimble & Reynolds, 1976; Trimble & Corbett, 1980).

Anticonvulsant polypharmacy has been considered inappropriate, as it can lead to more side-effects and the use of unnecessary medication, and behavioural difficulties and cognitive impairment are compounded (Reynolds, 1975; Shorvon *et al*, 1978; Shorvon, 1980). Moreover, it may be difficult to judge what overall effect may be obtained by adjustments to just one drug.

This paper reports the results of a systematic review of patients who were both epileptic and mentally handicapped. The primary aim was to provide optimum seizure control while reducing polypharmacy and the associated risks of side-effects.

Method

The population base for the study consisted of all in-patients of the Glenfrith Mental Handicap Unit in Leicestershire. In 1984, 738 in-patients were resident throughout 26 housing units variously scattered throughout Leicestershire, serving a population of 866 100.

At the outset of the study, data were obtained on all in-patient mentally handicapped patients who were either on medication for epilepsy, or who had sustained an epileptic convulsion within the previous two years. Such data included the patient's name, age, the types of medication received, including dose and frequency, the aetiology of the mental handicap (where known), associated medication, and the presumed seizure type. Data were obtained from a variety of sources, including staff, inspection of medical and nursing notes, epilepsy records, and drug cards. For 12 weeks we obtained from the existing recording system and in consultation with carers information about the type, frequency, and severity of seizures. These data acted as baseline information. Serum levels of phenytoin, phenobarbitone, valproic acid, and carbamazepine were analysed at the outset and throughout the study. Side-effects reported by the patients or their carers were recorded on the review sheet, after clinical assessment. Thereafter the anticonvulsant regime of all patients was reviewed jointly by a specialist in mental handicap and a specialist in clinical pharmacology. These reviews took place at regular intervals of 6, 12 or 26 weeks, until the patient had attained a 'steady state'; at this point it was considered that an optimum balance between seizure frequency, choice of medication, therapeutic dosage, and absence of medication side-effects had been achieved. The nature of the anticonvulsant drugs employed, their dose and serum concentration, and the relative frequency of seizures were compared between the initial state and the 'steady state'. Thereafter, an attempt was made at reviewing each patient on at least an annual basis.

In reviewing medication, the initial aim was to consolidate the medication already in use so as to ensure that full therapeutic doses were available. In the case of phenobarbitone and phenytoin, once-a-day administration was introduced. A change to a 'new' drug was contemplated only when side-effects of the current medication became evident, or adequate seizure control was not achieved. The serum anticonvulsant level and the optimum range proposed by the Clinical Pharmacology Laboratory for each medication were seen as valuable guidelines, but decisions about changes to medication took into account clinical response. Important factors were adverse reactions, effectiveness, and the ability of the patient to comply.

Results

The initial cohort consisted of 215 epileptics (58% male), who comprised 29% of the in-patient population of a group of hospitals for the mentally handicapped. The mean age of this population was 38 (s.d. 14) years. After the four-year study period, 43 patients had left the study (19 patients died, and 24 had been discharged as part of the policy of de-institutionalisation). The final cohort of 172 patients represented 80% of the initial cohort. The 43 patients lost to follow-up showed no statistical differences with respect to age, sex, degree of handicap, initial seizure frequency, or polypharmacy compared with the final cohort.

The total number of reviews undertaken on the whole cohort of 215 patients was 1058. The mean number of reviews undertaken per patient was 5.9 (s.d. 2.5), with a maximum of 11 reviews per patient.

The seizure frequencies at both the initial and final reviews are given in Table I. The number of patients who were free of fits had increased significantly by the end of the study ($\chi^2=27.62$, d.f. $=6$, $P<0.005$). This is accounted for by the improved seizure control of patients who initially sustained seizures infrequently. Patients who had frequent seizures remained difficult to control. Overall, seizure frequency was reduced in 48% of patients, increased in 33% of patients, and remained unchanged in 19%.

TABLE I
Seizure frequency

	Initial review		*Final review*	
	No. of patients	*%*	*No. of patients*	*%*
Seizure-free	37	22	71	41
Less than one seizure per year	52	30	24	14
Up to 4 seizures per year	36	21	27	16
Up to 1 seizure per month	18	10	15	9
Up to 1 seizure every fortnight	14	8	15	9
Up to 1 seizure per week	13	8	16	9
1 or more seizures per week	2	1	4	2

TABLE II
Number of anticonvulsants per patient

No. per patient	*Initially (%)*	*Finally (%)*
0	17 (9.9)	31 (18.0)
1	90 (52.3)	107 (62.2)
2	48 (27.9)	31 (18.0)
3	12 (7.0)	3 (1.7)
4	5 (2.9)	0 (0.0)
Mean	1.41	1.05

The number of different anticonvulsants used with each patient both initially and at the final review is given in Table II. The mean number of anticonvulsants given to each patient initially was 1.41. At the final review, the mean number of anticonvulsants given to each patient had decreased to 1.05. This is a statistically significant reduction of polypharmacy ($\chi^2=56.86$, d.f. $=16$, $P<0.005$). Eighty per cent of patients were maintained on either no anticonvulsant, or by the use of a single drug. Less than 2% of patients were maintained on combinations of more than two anticonvulsants.

Table III shows the changes in the prescriptions issued. There were significant reductions in the use of phenobarbitone, phenytoin, and sulthiame, but a significant increase in the use of carbamezepine and sodium valproate. Ethosuximide and primidone were withdrawn completely. When the patients were finally reviewed, over 90% of the anticonvulsant prescriptions issued were for just three drugs, namely carbamazepine (48.3%), phenobarbitone (23.9%) and sodium valproate (18.8%).

Among drugs taken in combination, there were significant reductions in phenobarbitone + phenytoin ($\chi^2=152.90$, d.f. $=1$, $P<0.005$), phenobarbitone + sodium valproate ($\chi^2=8.74$, d.f. $=1$, $P<0.005$), phenobarbitone + sulthiame ($\chi^2=48.55$, d.f. $=1$, $P<0.005$), and phenytoin + sodium valproate ($\chi^2=15.77$, d.f. $=1$, $P<0.005$).

Associated with the reduction in polypharmacy were increases in the doses of drugs employed, particularly of carbamazepine, phenobarbitone and sodium valproate (but not phenytoin) (Table IV).

TABLE III
Anticonvulsants employed

Anticonvulsant	*No. of prescriptions Initially*	*Finally*
Beclamide	1	1
Carbamazepine	60	85*
Clonazepam	3	3
Ethosuximide	6	0*
Phenobarbitone	62	42*
Phenytoin	33	9*
Primidone	8	0*
Sulthiame	20	3*
Sodium valproate	50	33*

*$P<0.005$.

TABLE IV
Initial and final mean daily doses of anticonvulsants

Drug	*Mean (s.d.) initial daily dose: mg*	*Mean (s.d.) final daily dose: mg*
Carbamazepine	735.44	940.96*
	(317.00)	(309.70)
Phenobarbitone	147.65	182.98**
	(81.45)	(64.78)
Phenytoin	313.33	313.89
	(143.79)	(61.36)
Sodium valproate	1171.40	1516.70*
	(504.67)	(632.20)

*$P<0.005$, **$P<0.05$.

TABLE V
Mean serum anticonvulsant concentrations (mg/l)

Anticonvulsant	*Initial concentration (s.d.)*	*Final concentration (s.d.)*
Carbamazepine	7.35	9.71*
	(2.49)	(2.63)
Phenobarbitone	24.54	28.80**
	(9.85)	(10.28)
Phenytoin	11.2	12.91
	(5.74)	(4.34)
Sodium valproate	63.82	70.95
	(23.74)	(18.28)

*$P<0.001$, **$P<0.05$.

For those patients who continued on the same anticonvulsant throughout the study, the increased doses of anticonvulsants prescribed were associated with increases in the mean serum concentrations of those drugs for which assay was available. The increases in serum concentrations of carbamazepine and phenobarbitone were statistically significant ($P<0.001$ and $P<0.05$ respectively). The mean increases in the serum concentrations of phenytoin and sodium valproate were not significant. These changes are shown in Table V.

Discussion

The systematic review of institutionalised patients with both mental handicap and epilepsy involved over a thousand separate reviews which took place within the patients' residential units. Visits to the wards for this purpose were generally welcomed and interest in the management of epilepsy increased.

The identification of seizure type presented difficulties. Nearly 80% of patients were considered to have generalised tonic–clonic seizures. The remaining 20% were considered to have petit mal, focal fits, myoclonic jerks, or a combination of seizure types. The identification of seizure type, other than tonic–clonic seizures, was difficult; it is likely also that tonic–clonic fits are over-represented by focal fits that became generalised. Our facilities for special observation and investigation of seizure type were minimal.

Our study has shown that it is possible to achieve a significant reduction in anticonvulsant polypharmacy in institutionalised mentally handicapped patients and effect a significant decrease in the frequency of seizures in some groups. Eighty per cent of patients were maintained either without anticonvulsant therapy or by the use of just one drug. Fewer than 2% of patients were maintained on more than two anticonvulsants. Carbamazepine, phenobarbitone and sodium valproate were found to be the most effective drugs clinically, while the use of beclamide, clonazepam, ethosuximide, phenytoin, primidone, and sulthiame was uncommon.

At the beginning of the study, a number of patients were found with serum anticonvulsant levels within the toxic range, while others had drug levels well below the accepted therapeutic range. These extreme positions were seen as cues for early action in order to achieve the rational use of medication.

At each review, careful inquiry was made to the carer for the emergence of side-effects; results were recorded on the review sheet. Side-effects included sedation, fluid retention associated with sodium valproate, rash and nausea with carbamazepine, ataxia and nystagmus with phenytoin, etc. They were all found to be reversible with either a reduction in drug dose or by a change in anticonvulsant.

Some patients would not take tablets, others refused syrup. The form and frequency of administration of the medication was a matter of negotiation between prescriber, patient, and carer. Two of the more able patients would not co-operate with any proposed changes of medication.

There have been few studies of the systematic management of epilepsy in patients with a mental handicap. This is perhaps surprising, in view of the known effects of anticonvulsant drugs on cognition, and the major difficulty of communication in this group. Fishbacher (1982) showed in a series of 36 mentally handicapped patients that it was possible to achieve a reduction in polypharmacy while at the same time reducing the frequency of epileptic seizures. He demonstrated that the reduction in number of drugs was associated with improvement in behaviour.

Sheppard *et al* (1987) studied the changes in anticonvulsant medication prescribed to an institutionalised mentally handicapped population over ten years. Polypharmacy reduction was not a major aim of their work, however. Their initial cohort of 179 patients in 1972 had fallen to 130 in 1982, of whom 52% were controlled on monotherapy.

While we have demonstrated a reduction in polypharmacy and an increase in the number of patients who were free from fits, there remained a small group who, in spite of everything, continued to take several drugs and whose seizures were exceedingly difficult to control. This group merits further study.

The association between psychiatric disorder and epilepsy, and especially between severe mental retardation and epilepsy, is noted in a document from the Department of Health and Social Security (1986) on services for people with epilepsy. The work described in this paper is in accord with one of the recommendations from that report: "People with both epilepsy and psychiatric disorder or mental handicap should receive proper assessment for their epilepsy, and this should not be overlooked where patients with a dual handicap are being managed within an institution". Careful review of anticonvulsant therapy is mandatory.

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References

CORBETT, J. A. (1981) Epilepsy and mental retardation. In *Epilepsy and Psychiatry* (eds E. R. Reynolds & M. R. Trimble). Edinburgh: Churchill Livingstone.

——, HARRIS, R. & ROBINSON, R. G. (1975) Epilepsy. In *Mental Retardation and Developmental Disabilities*, vol. VII (ed. J. Wortis). New York: Bruner Mazel.

DEPARTMENT OF HEALTH AND SOCIAL SECURITY (1986) *Report of the Working Group on Services for People with Epilepsy*. A report to the Department of Health and Social Security, the Department of Education and Science and the Welsh Office. London: HMSO.

DODRILL, C. B. & TROUPIN, A. S. (1977) Psychotropic effects of carbamazepine in epilepsy: a double blind comparison with phenytoin. *Neurology*, **27**, 1023–1028.

FISHBACHER, E. (1982) Effect of reduction of anticonvulsants on well-being. *British Medical Journal*, **285**, 423–424.

HIRTZ, D. G. & NELSON, K. B. Cognitive effects of anticonvulsant drugs. In *Recent Advances in Epilepsy* (eds T. A. Pedley & B. S. Meldrum). Edinburgh: Churchill Livingstone.

REYNOLDS, E. H. (1975) Chronic anti-epileptic toxicity: a review. *Epilepsia*, **16**, 319–334.

—— & TRAVERS, R. D. (1974) Serum anticonvulsant concentrations in epileptic patients with mental symptoms. *British Journal of Psychiatry*, **124**, 440–445.

SHEPPARD, L. C., BALLINGER, B. R. & FENTON, G. W. (1987) Anticonvulsant medication in a mental handicap hospital, 1972–1982. *British Journal of Psychiatry*, **150**, 512–517.

SHORVON, S. D. (1980) Monotherapy for epilepsy. *Irish Medical Journal* (suppl. 73), 36–41.

——, CHADWICK, D., GALBRAITH, A. W., *et al* (1978) One drug for epilepsy. *British Medical Journal*, *i*, 474–476.

SNAITH, R. P., JAMES, F. E. & WINOKUR, B. (1979) The drug treatment of mental illness and epilepsy in the mentally handicapped patient. In *Psychiatric Illness and Mental Handicap* (eds F. E. James & R. P. Snaith). London: Gaskell.

STORES, G. (1975) Behavioural effects of anti-epileptic drugs. *Developmental Medicine and Child Neurology*, **17**, 647–658.

THOMPSON, P., MUPPERT, F. A. & TRIMBLE, M. R. (1981) Phenytoin and cognitive function: effects on normal volunteers and implications for epilepsy. *British Journal of Clinical Psychology*, **20**, 155–162.

—— & TRIMBLE, M. R. (1982) Anticonvulsant drugs and cognitive functions. *Epilepsia*, **23**, 531–534.

TIZARD, J. & GRAD, J. C. (1961) *The Mentally Handicapped and their Families*. Maudsley monograph no. 7. London: Oxford University Press.

TRIMBLE, M. R. & REYNOLDS, E. H. (1976) Anticonvulsant drugs and mental symptoms; a review. *Psychological Medicine*, **6**, 169–178.

—— & CORBETT, J. A. (1980) Behaviour and cognitive disturbances in epileptic children. *Irish Medical Journal* (suppl. 73), 21–28.

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Perceived Parental Rearing Styles of Agoraphobic and Socially Phobic In-patients

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The perceived parental rearing practices and attitudes of agoraphobics, social phobics and non-patient normal controls were investigated, employing the EMBU, an inventory for assessing memories of upbringing. Findings obtained previously with out-patients were replicated with in-patients as subjects. Compared with the controls, agoraphobics rated both their parents as having been less emotionally warm but only their mothers as having been rejective. Socially phobic in-patients rated both their parents as having been rejective, as having lacked emotional warmth, and as having been over-protective. Comparisons between agoraphobics and social phobics showed differences in certain aspects of parental rearing, with the socially phobic in-patients assigning ratings more negatively than the agoraphobic group.

Atypical parental rearing characteristics have frequently been suggested as antecedents to phobic disorders. Negative rearing practices such as parental, particularly maternal, domination and over-protection, over-criticism by parents, and a lack of sufficient parental affection have been implied in agoraphobia (e.g. Webster, 1953; Tucker, 1956; Snaith, 1968; Shafar, 1976; Bowlby, 1980, pp. 292–312). However, while there appears to be much agreement among clinicians, who base their investigations on case reports or other descriptions of uncontrolled investigations, as to the role of such factors in the aetiology of agoraphobia (cf. Thyer *et al*, 1985; and Liotti, 1986), it is far more difficult to draw any conclusions from summaries of the available empirical evidence on family factors and agoraphobia (see Mathews *et al*, 1981, pp. 34–39; Foa *et al*, 1984; Tearnan *et al*, 1984; Thyer *et al*, 1985). Mathews *et al* (1981, p. 37), for example, are doubtful whether early family environment, including such factors as mentioned above, plays a part in predisposing individuals to developing agoraphobia, since not all studies agree in finding any significant distinguishing features. In their view, one important reason for the contradictory results is the use of different measuring instruments, many of which they suspect are of dubious validity (Mathews *et al*, 1981, p. 37). Related to this point of validity is what Tearnan *et al* (1984) have called the vagueness of the measures employed in the aetiological literature. They assert that the lack of specificity and clarity of definitions of parental rearing concepts that have been used may account for the inconsistencies in previous reports. In addition, they point out that measures need to be defined operationally to ensure a more reliable and valid assessment of parental rearing constructs. Thus, there is as yet no empirical evidence available (cf. Mathews *et al*, 1981, p. 35) for the contention (e.g. Andrews, 1966; Goldstein & Chambless, 1978; Wolfe, 1984) that, because of having been over-protected during childhood and adolescence, an individual learns a pattern of dependence on others that leaves him/her predisposed to develop agoraphobia as a method of coping with difficult situations later in life.

To judge from a recent review on social phobia by Liebowitz *et al* (1985), even less is known from empirical research about the possible aetiological role of negative parental rearing practices in the development of this disorder. In describing the theoretical link between shyness and self-presentation (i.e. the process by which individuals attempt to establish an identity by controlling the images of self available to others) and their aetiological aspects, Arkin *et al* (1986) suggested that a child punished (labelled inadequate) when his/her behaviour does not live up to high parental standards, and unrewarded when it does, may easily acquire an abiding ‘fear of failure’. Similarly, consistent rejection, or anticipated rejection, coupled with reinforcement of dependence in the child may produce anxiety and focus the child’s attention on avoiding disapproval rather than seeking approval (cf. Arkin *et al*, 1986). Canavan-Gumpert (1977) has shown that this attention to potential losses as opposed to potential gains engenders an increasingly conservative and hesitant response style. Arkin *et al* (1986) also noted that a reinforcement history which is insufficiently contingent could be an aetiological factor in the tendency to engage in self-critical ideation, and thus the aetiology of the protective self-presentational style. This protective style may manifest itself through withdrawal from social interaction, the adoption of neutral or conforming attitudes, self-handicaps, and modesty in attributions as a means of self-regulating feelings of social anxiety (cf. Arkin *et al*, 1986).

From the above, it can be concluded that there is some overlap in the 'typical' styles of upbringing of parents of individuals who become agoraphobic or socially phobic. Put somewhat differently, it is not clear which dimensions of parental rearing are specific for agoraphobia and which for social phobia (cf. also Liebowitz *et al*, 1985).

Relevant empirical data

To date, two empirical studies (Parker, 1979; Arrindell *et al*, 1983*b*) have appeared in which agoraphobics' and social phobics' perceptions of the rearing styles of their parents have been studied. These studies are discussed here because they meet the requirements that

(a) the patients have been compared with controls
(b) the measuring instruments used are reliable and valid measures of the major dimensions of parental rearing style (see Rollins & Thomas, 1979), and
(c) these major concepts have been clearly specified and defined.

Parker (1979) compared agoraphobics and social phobics with controls (selected consecutively from two general practices) on the Parental Bonding Instrument (PBI; Parker *et al*, 1979). The PBI is a self-administered 25-item questionnaire measuring the two principal dimensions of parental types of behaviour and attitudes, namely care (i.e. 'caring versus indifference/rejection') and over-protection (i.e. 'control/over-protection versus allowance of autonomy and independence'). Descriptions of the measuring concepts and data supporting their reliability and validity are given in Parker *et al* (1979) and Parker (1983*a*,*b*). Parker (1979) found that those assigned to a socially phobic group rated both parents as less caring and as more protective, while those assigned to an agoraphobic group differed from controls only in reporting less maternal care.

Arrindell *et al* (1983*b*) studied the perceived parental rearing styles of social phobics, agoraphobics and height (simple) phobics by comparing their ratings of their parents with those of non-patient normal controls, employing the EMBU (*Egna Minnen Beträffande Uppfostran*; "My memories of upbringing"; Perris *et al*, 1980). The EMBU is an 81-item self-administered inventory which measures the factorially-derived dimensions of rejection, emotional warmth, over-protection and favouring subject (not used here). The EMBU rejection and emotional warmth dimensions correspond to the PBI care dimension, while the EMBU over-protection dimension is conceptually similar to the similarly named dimension of the PBI (see the Method section for a description of the different aspects that are incorporated in the PBI and the EMBU). Data supporting the reliability and the validity of the EMBU are given in Arrindell *et al* (1983*a*), Arrindell & van der Ende (1984) and Arrindell *et al* (1986*a*).

Arrindell *et al* (1983*b*) found that compared with controls from the general population, both social phobics and height phobics rated both parents as lacking in emotional warmth and as having been rejective and over-protective. Agoraphobics differed from controls only in that they rated both parents as having lacked emotional warmth and only their mothers as having been rejective. Thus, agoraphobics did not differ from normal controls in terms of parental protectiveness or paternal rejection. It was further pointed out by Arrindell *et al* (1983*b*) that, to judge from the magnitudes of the differences found (effect sizes), certain parental rearing characteristics might be more typical for one type of phobic disorder than another. A secondary analysis of the findings of Arrindell *et al* (1983*b*) showed that agoraphobics and social phobics differed from each other in terms of paternal rejection only, the socially phobic group having the highest mean rating in this respect (small effect size, $d=0.22$).

The study

Whereas Arrindell *et al* (1983*b*) made use of phobic subjects who were treated on an out-patient basis, the present study was aimed at partly repeating that study by using agoraphobic and socially phobic in-patients as subjects. In addition, it extended that study by performing comparisons between agoraphobic and social phobics on the EMBU subscales and by examining between-group differences in terms of ratings of consistency and strictness of parental rearing. These were assessed with two additional questions from the EMBU.

Since it could not be assumed that data produced in one type of sample (out-patients) would by definition generalise to another type of sample (in-patients), it was thought wiser to take both clinical–theoretical viewpoints and empirical data (Parker, 1979; Arrindell *et al*, 1983*b*) as bases from which to formulate hypotheses for the present clinical groups. In addition, it could be argued (Parker, 1979) that the association between negative rearing practices and phobic condition could turn out to be stronger with increasing psychopathology in recipients, meaning in this context that findings obtained previously with out-patients might result as less marked than those yielded with patients carrying the same diagnostic label but treated on an in-patient basis.

In reviewing the descriptive evidence on pathogenic patterns of family interaction in agoraphobia, Bowlby (1980) has pointed to the dominant and controlling or over-protective role that parents, usually mothers, played in the genesis of the target symptoms. In addition, Bowlby (1980) attests to the possible causal role of threats of rejection and actual rejection in the agoraphobic patient's condition. Over-criticism by parents and lack of parental affection are other aspects that have been raised in the literature on agoraphobia (e.g. Tucker, 1956). Bowlby (1980) also described the style of upbringing in the families of agoraphobic patients as inconsistent. He writes: "not infrequently, a parent who gives the impression of being consistently over-protective is found on occasion to be exactly the reverse; while a parent who appears to be consistently rejecting can on occasion be affectionate; the behaviour of the parents of many agoraphobics is probably very often intensely ambivalent" (p. 308). Bowlby (1980) does not make any direct mention of any clinical evidence of a pattern of strict upbringing in the parental homes of agoraphobic patients, although repeated references to the observation that a substantial proportion of agoraphobic patients have been subjected to harsh treatment – a mother, for instance, is described as a 'tartar' who had always used the most dreadful and violent threats, including outright rejection, to get her own way – make it likely that the pattern does occur. Thus, it was hypothesised that agoraphobics would differ from normal controls in having lower ratings for parental affection, and higher ratings for parental protection, rejection, inconsistency and strictness.

On the basis of the theoretical viewpoints of Arkin *et al* (1986) with respect to the aetiological part played by negative rearing styles in social phobia outlined earlier, it was anticipated that social phobics would also rate significantly higher than their normal control equivalents on strictness and inconsistency of parental rearing behaviour. Furthermore, Arkin *et al* (1986) have theorised that consistent rejection, or anticipated rejection, paired with reinforcement of dependence in the recipient is associated with social phobia. Thus, both parental rejection and parental protection were postulated to differentiate social phobics from their normal control counterparts, the former group having the higher mean ratings.

In addition, the empirical studies by Parker (1979) and Arrindell *et al* (1983*b*) suggested that social phobics could be differentiated from normal controls by the former's lower parental affection ratings, and that the differential pattern in findings obtained when comparing phobic types with normal controls would argue for differentiation between agoraphobic and socially phobic in-patients by different measures of style of upbringing.

Method

Subjects and procedures

The in-patients were 43 agoraphobics and 16 social phobics consecutively admitted for treatment in various clinical trials at a non-university hospital department of behavioural psychotherapy during 1984–86. All patients met the DSM-III criteria (American Psychiatric Association, 1980) for agoraphobia or social phobia as a major disorder, based on consensus between a clinical psychologist and a psychiatrist. The controls were 100 randomly selected non-patients from a general population sample comprising subjects who had volunteered to participate in a study concerned with the development of measures for use in mental health research. The original main sample (cf. Arrindell *et al*, 1984) was a volunteer subsample taken from a larger randomly-drawn community-based Dutch sample. Since this subsample comprised volunteers (age range: 20–69 years), it, of course, does not constitute a truly random sample; at most one might refer to the sample as fortuitous, i.e. collected in such a way as to maximise diversity, but relying on chance rather than design.

Eysenck (1975) discusses the concept of a fortuitous but reasonable sample as opposed to a random or quota sample, and has empirically demonstrated in a further study that a reasonable sample gives results that are very similar (in some instances even identical) to those obtained when using a proper quota sample (Eysenck, 1979).

A multitude of background demographic and other data were obtained for each subject. These included, among other variables, sex, age, education, number of siblings, birth order, and age at departure from the parental home. Since the groups were fairly well comparable in terms of these variables – except for age (see below) – and because of the lack of any meaningful associations between these variables and the EMBU ratings, data with respect to sex and age only were deemed relevant in presenting a brief description of the samples.

The distribution according to sex was as follows: 53.5% males and 46.5% females in the agoraphobic sample, 56.3% and 43.8% respectively for the socially phobic males and females, and 54% and 46% respectively for the normal males and females (overall $\chi^2 < 1$, d.f. = 2, $P > 0.50$, NS). The groups of agoraphobics and social phobics were comparable in terms of mean age: 32.9 years for both groups. However, they were significantly younger than the normal controls, whose mean age was 41 (overall $F = 9.38$, d.f. = 2, $P < 0.001$). The influence of age on the outcome of the data analysis will be examined closely below.

The EMBU

At the item-level, the EMBU comprises 14 aspects of parental rearing types of behaviour and attitudes: abusive, depriving, punitive, shaming, rejecting, over-protective, over-involved, tolerant, affectionate, performance oriented, guilt engendering, stimulating, favouring subject and favouring siblings (Perris *et al*, 1980). These a priori aspects have been shown to reduce to four replicable and invariant dimensions: rejection, emotional warmth, over-protection, and favouring subject (e.g. Arrindell & van der Ende, 1984). Since there is some evidence indicating that the favouring subject factors are specific to Dutch samples – that is, they are not generalisable to a number of national groups other than the Dutch (Arrindell *et al*, 1986*a*; Arrindell *et al*, 1986*b*) – these were deleted from the present investigation.

A brief outline of the correspondence between the EMBU and the PBI is in order. The EMBU rejection and emotional warmth dimensions correspond to the PBI care dimension in that the latter involves one pole defined by affection, emotional warmth, empathy and closeness, and the other defined by emotional coldness, indifference and neglect. The EMBU over-protection dimension overlaps with the PBI over-protection dimension since the latter has one pole defined by control, over-protection, intrusion, excessive contact, infantilisation and prevention of independent behaviour, and the other defined by items that suggest allowance of independence and autonomy. A critical examination of the validity of content of the EMBU (Arrindell & van der Ende, 1984) revealed that the ingredients judged to be salient in measuring the major components of parental rearing (Rollins & Thomas, 1979) are fairly well represented in the questionnaire. In fact, Liotti (1986) has recently asserted that the EMBU is informationally (i.e. in terms of validity of content) superior to the PBI in this respect.

It is important to note that the background variables mentioned earlier (including age, for which the present patient samples differed from controls) have generally been found to be uncorrelated or only negligibly so with rearing aspects (e.g. Arrindell *et al*, 1983*a*, 1986*a*; cf. also Fishbein, 1984, pp. 73–77). This observation holds for the present in-patient samples as well (Arrindell *et al*, 1989). In addition, the EMBU scales have been reported to be negligibly associated with social desirability (Arrindell *et al*, 1983*a*). The questionnaire was completed by the patients as part of both a diagnostic and a research programme before the start of treatment.

Statistical analyses

One-tailed univariate *t*-tests were performed throughout. Where evidence for non-homogeneity was clearly marked ($P \leq 0.01$, two-tailed tests), *t*-values adjusted for unequal variances were calculated.

The influence of age on the outcome of the data analysis was examined, and analyses of covariance (ANCOVAs) were performed for each variable for those comparisons that involved agoraphobics or social phobics against normal controls, since the former two groups differed meaningfully in terms of age from the latter group (agoraphobics and social phobics were comparable in terms of mean age). In the ANCOVAs, the influence of age on the results was partialled out. The findings obtained from these analyses were compared with those obtained from the multiple *t*-tests conducted without elimination of any age effects. The working α was set at 0.05.

Where data are missing (because individuals had no brothers or sisters or because they gave ratings for only one parent) the values of N in the different analyses inevitably differ, but only slightly so, from those given in the Subjects section above (see the appropriate tables).

Results

Preliminary analyses

In both patients and normal controls, correlations between age and the EMBU variables were negligible (i.e. very close to zero) and of magnitudes comparable to those reported in Arrindell *et al* (1989). The results obtained with and without partialling out for the influence of age did not differ appreciably: identical conclusions were obtained across these analyses. Therefore, the simple *t*-tests are reported below.

Main analyses

Table I summarises the means and standard deviations for ratings for each group for each dimension, including the general ratings of strictness and consistency, for each parent.

Agoraphobics or social phobics v. normal controls

The one-tailed *t*-test comparing agoraphobics with normal controls on each of the EMBU scales showed the former group to differ significantly, and in the expected direction, from the control group, for the fathers' emotional warmth ($t = -3.33$, d.f. = 136, $P < 0.001$), the mothers' rejection ($t = 2.46$, d.f. = 61, $P < 0.01$) and emotional warmth ($t = -4.05$, d.f. = 137, $P << 0.001$) scales.

Social phobics rated both their fathers and their mothers as more rejective than normal controls rated theirs (*t*-values respectively 3.17, d.f. = 16, $P < 0.01$, and 4.93, d.f. = 110, $P << 0.001$). In addition, the social phobics rated both parents significantly lower on emotional warmth than the controls rated theirs (*t*-values respectively -4.19, d.f. = 109, and -5.25, d.f. = 110, *P*-values $<< 0.001$). Both groups could be distinguished from each other in terms of protection as well, the socially phobic group having rated both their parents as more protective than the control group rated theirs (*t*-values respectively 1.85, d.f. = 109, $P = 0.03$, and 2.03, d.f. = 110, $P = 0.02$).

The following picture emerged with respect to the consistency and strictness ratings: compared with normal controls, the agoraphobic in-patients reported both their parents as having brought them up in a less consistent fashion than the normal controls reported theirs as having raised them (*t*-values for the fathers and the mothers were respectively 2.42, d.f. = 132, $P = 0.01$, and 3.34, d.f. = 56, $P < 0.001$). In addition, the agoraphobics reported their fathers as having been less strict than the normal controls reported theirs as having been ($t = 2.08$, d.f. = 133, $P = 0.02$).

As a group, social phobics rated the rearing behaviour of both their fathers and their mothers as less consistent

TABLE I

*Ratings for each parental rearing measure, for each subject sample**

	Rejection	*Emotional warmth*	*(Over-)protection*	*Inconsistency*	*Lack of strictness*
Ratings for fathers					
Agoraphobics					
Mean	36.70	43.67	32.72	2.14	3.00
s.d.	9.87	11.29	9.14	0.68	0.88
Social phobics					
Mean	45.06	37.75	35.31	2.13	2.50
s.d.	13.49	12.77	9.87	0.62	1.03
Normal controls					
Mean	34.11	50.43	31.77	1.86	2.68
s.d.	7.16	10.93	6.56	0.60	0.81
Ratings for mothers					
Agoraphobics					
Mean	41.12	44.81	34.98	2.48	3.02
s.d.	13.85	12.50	8.95	0.89	0.81
Social phobics					
Mean	48.63	38.44	38.88	2.50	2.81
s.d.	11.14	11.27	7.63	0.89	0.91
Normal controls					
Mean	35.39	52.88	34.98	1.98	2.91
s.d.	9.75	10.01	7.04	0.55	0.77

**N* (EMBU subscales): agoraphobics, 43; social phobics, 16; normal controls, 95–96. *N* (EMBU general ratings): agoraphobics, 42; social phobics, 16; normal controls, 92–94.

Note. Theoretical ranges for consistency and strictness ratings are 1 (very consistent or very strict style) to 4 (very inconsistent or totally non-strict style of upbringing).

than normal controls rated the rearing behaviour of their parents (t-values respectively 1.62, d.f. = 106, $P = 0.05$ and 2.26, d.f. = 17, $P = 0.02$).

Agoraphobics v. social phobics

Comparison of agoraphobics with social phobics, on the EMBU subscales, showed clear differences in terms of both the fathers' and the mothers' rejection ratings: social phobics rated both parents as *more* rejective than agoraphobics rated theirs (t-values respectively -2.61, d.f. = 57, $P < 0.01$, and -1.94, d.f. = 57, $P = 0.03$). In addition, significantly lower mean ratings were yielded for social phobics when compared with agoraphobics in terms of paternal and maternal affection: ratings of the fathers, $t = 1.73$, d.f. = 57, $P = 0.04$; ratings of the mothers, $t = 1.79$,

TABLE II

Degree of relevancy of significant differences encountered between agoraphobics, social phobics, and normal controls in recollections of types of parental rearing behaviour and attitudes (Cohen's measure |d| of effect size)

	Agoraphobics (A) *v.* *normal controls (N)*	*Social phobics (S)* *v.* *normal controls (N)*	*Agoraphobics (A)* *v.* *social phobics (S)*
Father's style			
Rejection	–	1.01 (S>N)	0.71 (S>A)
Emotional warmth	0.61 (A<N)	1.07 (S<N)	–
Over-protection	–	0.42 (S>N)	–
Inconsistency	0.44 (A>N)	0.44 (S>N)	–
Lack of strictness	0.38 (A>N)	–	0.52 (A>S)
Mother's style			
Rejection	0.48 (A>N)	1.26 (S>N)	0.60 (S>A)
Emotional warmth	0.71 (A<N)	1.35 (S<N)	–
Over-protection	–	0.53 (S>N)	–
Inconsistency	0.68 (A>N)	0.70 (S>N)	–
Lack of strictness	–	–	–

Note. For purposes of interpretation, Cohen (1977, p. 40) considers 0.20 *small*, 0.50 *medium*, and 0.80 *large*.

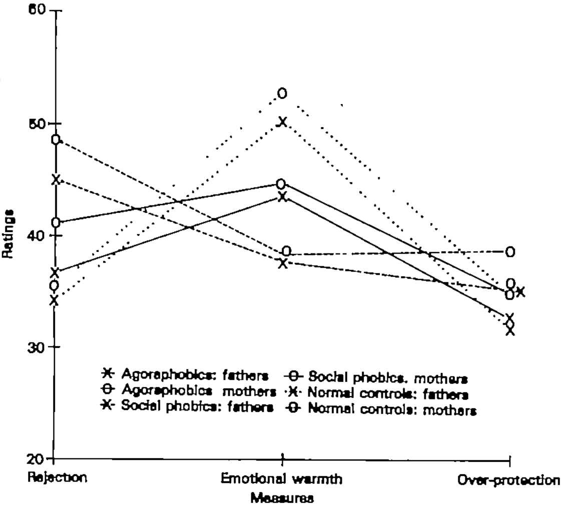

FIG. 1 EMBU subscale profile (based on mean ratings) of non-patient normal controls, and of agoraphobic and socially phobic in-patients.

d.f. = 57, $P = 0.04$. No distinctions could be made between these groups in terms of parental protection: fathers' data, $P = 0.17$; and mothers' data, $P = 0.06$.

For the general ratings, the groups of patients differed in terms of paternal strictness only where social phobics rated their fathers' rearing style as more strict than agoraphobics rated theirs ($t = 1.84$, d.f. = 56, $P < 0.05$).

Table II gives, for each measure, a survey of the magnitudes of the statistically significant differences that were obtained. These were estimated, using Cohen's (1977, p. 40) measure *d* of effect size. Another way of clarifying the findings is to depict the means for each group for each variable graphically. This is done for the EMBU subscales in Fig. 1, while the means on the general ratings are given in Fig. 2.

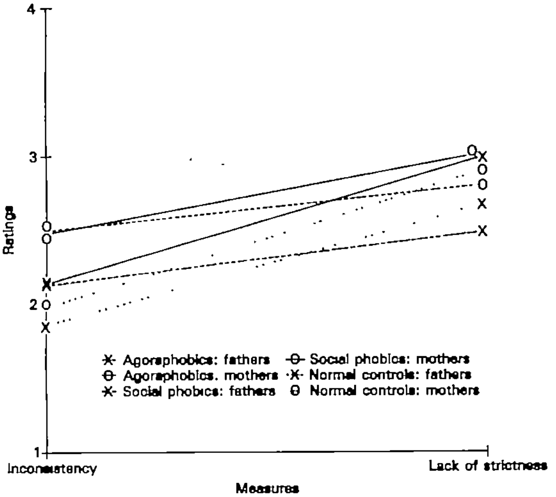

FIG. 2 EMBU consistency and strictness profile ratings (based on mean ratings) of non-patient normal controls, and of agoraphobic and socially phobic in-patients.

Further analyses

For the variables dealing with consistency and strictness of parental upbringing, agoraphobics and social phobics differed in terms of paternal strictness only. To examine this difference more closely, the correlation between paternal strictness and each of the paternal EMBU dimensions was determined for each of the groups of patients and for the controls (see Table III). The overall picture that emerges from this table is that greater paternal strictness is associated with lower ratings for emotional warmth, and higher ratings for rejection and protection.

When the magnitudes of the effect sizes are taken into account (disregarding whether differences in correlations are statistically significant or not, which to a large extent depends on sample size), three notable differences emerge (Table III). The association between paternal strictness and

(a) paternal rejection is more marked in the socially phobic group (72% of the variance in either of the two variables may be attributed to the variance of the other) than in the agoraphobic (34% shared variance) or normal controls sample (31%)

(b) paternal affection is also more marked in the socially phobic group (29%) than in the agoraphobic (4%, a statistically non-significant correlation) or normal sample (10%)

(c) paternal protection is not significant in the socially phobic group, moderately associated (12%) in the normal control sample, and sizeably so (37%) in the agoraphobic group.

TABLE III

The associations between paternal strictness and each of the paternal EMBU dimensions in each subject sample

	Agoraphobics N = *42*	*Social phobics* N = *16*	*Normal controls* N = *93*
Father's			
Rejection	0.58**	0.85**	0.56**
Emotional warmth	−0.21	−0.54*	−0.32**
Over-protection	0.61**	0.20	0.34**

* $P \leq 0.05$, ** $P \leq 0.01$ (Pearson's *r*, one-tailed tests).

Note. For purposes of interpretation, Cohen (1977, p. 9) considers 0.10 *small*, 0.30 *medium*, and 0.50 *large* effect sizes.

Strictness is rated here as 1 = not at all strict, and 4 = severely strict.

Discussion

Generalisability of previous findings

A total of 39 statistical tests were performed in the present investigation. The number of statistically significant findings that were produced (24) clearly exceeded what one would expect on the basis of chance alone (2).

The present findings obtained with in-patients formed an exact replication of those obtained with agoraphobics and social phobics who were treated on an out-patient basis, when compared with non-patient controls (Parker, 1979; Arrindell *et al*, 1983*b*). Agoraphobic in-patients rated both their fathers and their mothers as having been less emotionally warm but only their mothers as having been rejective. The magnitudes of the differences found here were in close agreement with those obtained by Arrindell *et al* (1983*b*). Socially phobic in-patients rated both their parents as having been rejective, as having lacked emotional warmth and as having been over-protective. The magnitudes of these differences were, for the rejection and emotional warmth dimensions, somewhat higher than the corresponding effect sizes reported in our previous study with out-patients. Thus, the findings obtained with socially phobic individuals were in line with expectations formulated by Parker (1979) and Arkin *et al* (1986). Parker (1979) notes that,

> "It would appear reasonable to suggest that a child exposed to parental characteristics of low care and overprotection, which inhibit the development of a satisfying parent–child bond, might subsequently experience greater difficulty in interpersonal situations and experience anxiety in social situations. Parental overprotection, by restricting the usual developmental process of independence, autonomy and social competence, might further promote any diathesis to a social phobia" (p. 559).

Although most clinicians share similar views with respect to the role of parental, particularly maternal, over-protection in the genesis of agoraphobia (cf. Mathews *et al*, 1981, p. 35), the present controlled study, in which reliable and valid measures of the major dimensions of parental rearing style have been used, appears as the third in a row which fails to support such a contention. It does underscore the view that maternal rejection and lack of maternal warmth might be crucial factors in the genesis of agoraphobia (cf. Bowlby, 1980, e.g. p. 307). In addition, the possible role of the fathers' lack of an emotionally warm relationship with the recipient in the background of agoraphobia was highlighted.

Extension of previous findings

A secondary analysis of the findings of Arrindell *et al* (1983*b*) showed that paternal rejection might be a factor distinguishing agoraphobic out-patients from socially phobic patients, the latter having the highest mean rating. This finding was replicated here too, the magnitude of the difference being larger for in-patients (0.71) than for out-patients (0.22). In addition, maternal rejection discriminated between the two groups of in-patients, the difference – social phobics having a higher average rating than agoraphobics – being of *medium* effect size.

As hypothesised, both agoraphobics and social phobics reported their fathers' and their mothers' style of upbringing as more inconsistent than normal controls indicated theirs to have been. Contrary to expectations, however, agoraphobics reported their fathers' rearing style as less strict (*small* difference) compared with controls. Maternal strictness did not differentiate patients from controls. The only variable out of four strictness and consistency measures that distinguished agoraphobics from social phobics was the latter's higher average rating for paternal strictness. Higher inconsistency ratings for both parents of socially phobic in-patients appeared to tally with the assertion of Arkin *et al* (1986) – based on work by Canavan-Gumpert (1977) and Teevan and McGhee (1972) – that a child punished when his/her behaviour does not meet high parental standards, and unrewarded when it does, may easily acquire an enduring 'fear of failure'. Our findings are also in close agreement with the contention of Arkin *et al* (1986) that a reinforcement history that is insufficiently contingent might be of aetiological significance in psychological states and traits of social anxiety. Arkin *et al* (1986) point out that:

> "The individual who has suffered a chaotic or capricious reinforcement history may have difficulty discerning what rewards have been for, and may therefore view 'ill-gotten gains' as precarious and likely to be unattainable in the future. Even if abundant, the rewards are uninformative concerning one's competence. This set of circumstances would . . . place one's sense of self-worth at risk" (p. 196).

That inconsistency of parental rearing behaviour and attitudes is not only characteristic of social phobics but also typical of agoraphobics may relate to the fact that the latter, as is true of the former, have also been reported to be to some extent more socially anxious and less expressive than other patients and/or normal controls (cf. Chambless & Goldstein, 1980; Chambless, 1982; Arrindell & Emmelkamp, 1987).

Apparently, in line with descriptions of the parental background of socially phobic patients offered by Arkin *et al* (1986), paternal strictness and paternal rejection appeared in the present study as a distinguishing feature between the phobic types considered, in that

(a) the sizeable correlation ($r=0.85$) that was observed between the two variables was clearly more marked in socially phobic than in both agoraphobic in-patients and normal controls, and
(b) agoraphobics and social phobics could be distinguished on the basis of both variables.

More on specificity of factors

To date, straightforward empirical findings to indicate that certain aspects of upbringing are more specific for social phobia than for other phobias have been lacking in the research literature (Liebowitz *et al*, 1985). The present study found that ratings for paternal and maternal rejection and paternal strictness differentiated agoraphobics from social phobics, the latter group having the highest mean ratings in these terms. In addition, lower mean ratings were obtained for social phobics when compared with agoraphobics in terms of paternal and maternal affection. Further, greater paternal strictness was more effectively associated with more paternal rejection practices and greater lack of paternal affection (emotional warmth) in social phobics than in agoraphobics. Also, a more strict paternal rearing style was more strongly associated with greater paternal protection in agoraphobics than in social phobics, this association having appeared to be relatively non-existent in the latter group of subjects. Thus, one's own perceptions of one's parents' rearing behaviour appeared here to be *another* set of variables (see Amies *et al*, 1983; Liebowitz *et al*, 1985; Persson & Nordlund, 1985; Solyom *et al*, 1986) in which social phobia was distinguishable from the agoraphobic subtype. This finding underscores further the necessity of differentiating between the different phobic subtypes (Marks, 1969; Emmelkamp, 1982; Amies *et al*, 1983). However, compared with normal controls, higher ratings for the EMBU rejection and protection dimensions and lower ratings for the emotional warmth construct have been obtained for other (non-phobic) patient groups as well (e.g. Hoekstra *et al*, 1989; Emmelkamp & Heeres, 1988). Emmelkamp & Heeres (1988), for example, reported that drug addicts could be distinguished from normal controls in terms of paternal and maternal rejection, affection and protection, the former group assigning ratings in a more negative direction than the latter. There are differences, however, between these different studies with respect to the magnitudes of the observed differences. For example, the magnitude of effect size for ratings of maternal emotional warmth in the comparison involving drug addicts and controls was *small*, whereas, in the present study, the corresponding difference between socially phobic in-patients and normal controls was *very large*. Thus, certain types of rearing behaviour and attitudes may have greater aetiological significance for one disorder than for another.

Final points

Parental rearing practices were not directly assessed here but were rated by the patient. It could be argued that such an indirect test may raise the possibility of one's memories producing a distorted view of one's parents' rearing behaviour rather than reflecting actual rearing practices. Wolkind & Coleman (1983) have suggested that any measure whose rating depends solely on the direct response of the subject may give misleading results; and that any study using such measures should be treated with caution. Wolkind & Coleman (1983) base their cautionary note on their empirical study which showed that while in a sample of young mothers an association was found between a depressed mood and the recall of poor parental relationships during childhood, among those women who had been depressed but had recovered by the time of questioning, no recalls of a poor relationship were given. In addition, a second retrospective measure of childhood experience, based on more factual details, was *un*related to current mental state. The findings of Wolkind & Coleman (1983) are, however, not in line with results from other investigations showing that retrospective reports made by adolescents and adults concerning their parents' behaviour and attitudes during childhood relate substantially to independent measures of these experiences (e.g. Bronson *et al*, 1959; Rosenthal, 1963; Solyom *et al*, 1976; Parker, 1984), thus implying that these self-histories may be interpreted as measures of the phenomenological impact of types of parental behaviour (Burger *et al*, 1975). In addition, Perris *et al* (1986, p. 174) have recently pointed out that, practically three decades ago, Ausubel avowed that what is relevant is not how rearing practices have really been, but how they were perceived by the subject undergoing such practices. Furthermore, it can be argued (Lewinsohn & Rosenbaum, 1987) that for clinicians the most important thing is how their clients construe their past, not how it really was (see also Richman & Flaherty, 1987). Knowing which factors affect the quality of recall of parental rearing behaviour then becomes more important than obtaining corresponding independent objective indicators of such behaviour. Lewinsohn & Rosenbaum (1987), for example, have suggested that the endorsement frequencies of ratings of subjects on scales that assess recall of parental behaviour may depend on the negative or positive connotations of the items that make up such measures. They recommend that in future empirical studies independent raters evaluate the extent to which this is true. Further, one's memories may be distorted by mood – that is, one's memories may be 'mood-state dependent' (Bower, 1981). In line with many previous studies (cf. Blaney, 1986; Bower, 1981), Lewinsohn & Rosenbaum (1987) found empirical support for the hypothesis that the current depressive state of individuals, and not their past experiences with depression, influences the degree to which *negative* aspects of their parents (e.g. rejection) are recalled. However, they point out that future investigations should demonstrate that these negative aspects wax and wane with changes over time in the subjects' state of depression.

An additional issue is, of course, that the most secure knowledge in developmental psychology comes from large-scale, longitudinal study of groups of people over many years (e.g. Fishbein, 1984, p. 45). A final test of the developmental model awaits such a direct, prospective investigation. This, however, will be difficult to realise on practical grounds. In the mean time, the present findings point to the necessity of considering those parental rearing factors that have been replicated across cross-sectional studies in aetiological models of agoraphobia and social phobia. Because of the complex essential qualities of phobic disorders, such models (Mathews *et al*, 1981; Chambless, 1982; Emmelkamp, 1982; Foa *et al*, 1984; Hallam, 1985; Marks, 1987) are multifactorial in nature with attention necessarily directed to developmental, cognitive, conditioning, social and biological factors as well as the interdependence of these factors. Another reason for considering the relevancy of such data despite their retrospective character is that one's recalled early relationship with one's parents has been shown to be among the prognostic factors related to treatment outcome in phobic disorders in adulthood (Persson *et al*, 1984).

Further studies are needed to examine an aspect of parental rearing not considered here, but which is very likely to be related to the higher-order dimension of care (rejection v. emotional warmth), namely explicit or implicit threats of abandonment or suicide by one or both parents as a way of disciplining a child. Such a factor has been implied by Bowlby (e.g. 1980, e.g. pp. 292–312) as one of the many different parental support factors that may be operative in the background of agoraphobia (Liotti, 1986, p. 115; but see Thyer *et al*, 1985).

References

American Psychiatric Association (1980) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn). Washington DC: APA.

Amies, P. L., Gelder, M. G. & Shaw, P. M. (1983) Social phobia: a comparative clinical study. *British Journal of Psychiatry*, **142**, 174–179.

Andrews, J. D. W. (1966) Psychotherapy of phobias. *Psychological Bulletin*, **66**, 455–480.

Arkin, R. M., Lake, E. A. & Baumgardner, A. H. (1986) Shyness and self-presentation. In *Shyness: Perspectives on Research and Treatment* (eds W. H. Jones, J. M. Cheek & S. R. Briggs). New York: Plenum Press.

Arrindell, W. A. & Emmelkamp, P. M. G. (1987) Psychological states and traits in female agoraphobics: a controlled study. *Journal of Psychopathology and Behavioral Assessment*, **9**, 237–253.

—— & van der Ende, J. (1984) Replicability and invariance of dimensions of parental rearing behaviour: further Dutch experiences with the EMBU. *Personality and Individual Differences*, **5**, 671–682.

——, Emmelkamp, P. M. G. & van der Ende, J. (1984) Phobic dimensions: I. Reliability and generalizability across samples, gender and nations. *Advances in Behaviour Research and Therapy*, **6**, 207–254.

——, ——, Brilman, E., *et al* (1983*a*) Psychometric evaluation of an inventory for assessment of parental rearing practices: a Dutch form of the EMBU. *Acta Psychiatrica Scandinavica*, **67**, 163–177.

——, ——, Monsma, A., *et al* (1983*b*) The role of perceived parental rearing practices in the aetiology of phobic disorders: a controlled study. *British Journal of Psychiatry*, **143**, 183–187.

——, Methorst, G. J., Kwee, M. G. T., *et al* (1989) Expanding the validity of a measure of reported parental rearing practices with psychiatric inpatients; further Dutch experiences with the EMBU. *Personality and Individual Differences*, **10**, 493–500.

——, Perris, C., Eisemann, M., *et al* (1986*a*) Cross-national generalizability of patterns of parental rearing practices: invariance of EMBU dimensional representations of healthy subjects from Australia, Denmark, Hungary, Italy and the Netherlands. *Personality and Individual Differences*, **7**, 103–112.

——, ——, Perris, H., *et al* (1986*b*) Cross-cultural invariance of dimensions of parental rearing behaviour: comparison of self-ratings of Swedish depressives and healthy subjects with Dutch target ratings on the EMBU. *British Journal of Psychiatry*, **148**, 305–309.

Blaney, P. H. (1986) Affect and memory: a review. *Psychological Bulletin*, **99**, 229–246.

Bower, G. H. (1981) Mood and memory. *American Psychologist*, **36**, 129–148.

Bowlby, J. (1980) *Attachment and Loss, Volume II. Separation: Anxiety and Anger*. London: The Hogarth Press and The Institute of Psycho-Analysis (reprinted with corrections).

Bronson, W. C., Katten, E. S. & Livson, N. (1959) Patterns of authority and affection in two generations. *Journal of Abnormal and Social Psychology*, **58**, 143–152.

Burger, G. K., Armentrout, J. A. & Rapfogel, R. G. (1975) Recalled parental behavior and objective personality measures: a canonical analysis. *Journal of Personality Assessment*, **39**, 514–522.

CANAVAN-GUMPERT, D. (1977) Generating reward and cost orientations through praise and criticism. *Journal of Personality and Social Psychology*, **35**, 501–513.

CHAMBLESS, D. L. (1982) Characteristics of agoraphobics. In *Agoraphobia: Multiple Perspectives on Theory and Treatment* (eds D. L. Chambless & A. J. Goldstein). New York: Wiley.

—— & GOLDSTEIN, A. J. (1980) Anxieties: agoraphobia and hysteria. In *Women and Psychotherapy: An Assessment of Research and Practice* (eds A. M. Brodsky & R. T. Hare-Mustin). New York: The Guilford Press.

COHEN, J. (1977) *Statistical Power Analysis for the Behavioral Sciences* (revised edn). New York: Academic Press.

EMMELKAMP, P. M. G. (1982) *Phobic and Obsessive–Compulsive Disorders; Theory, Research, and Practice*. New York: Plenum Press.

—— & HEERES, H. (1988) Drug addiction and parental rearing style: a controlled study. *The International Journal of the Addictions*, **23**, 207–216.

EYSENCK, H. J. (1975) Who needs a random sample? *Bulletin of the British Psychological Society*, **28**, 195–198.

—— (1979) Personality factors in a random sample of the population. *Psychological Reports*, **44**, 1023–1027.

FISHBEIN, H. D. (1984) *The Psychology of Infancy and Childhood: Evolutionary and Cross-Cultural Perspectives*. Hillsdale, New Jersey: Lawrence Erlbaum Associates.

FOA, E. B., STEKETEE, G. & YOUNG, M. C. (1984) Agoraphobia: phenomenological aspects, associated characteristics, and theoretical considerations. *Clinical Psychology Review*, **4**, 431–457.

GOLDSTEIN, A. J. & CHAMBLESS, D. L. (1978) A reanalysis of agoraphobia. *Behavior Therapy*, **9**, 47–59.

HALLAM, R. S. (1985) *Anxiety: Psychological Perspectives on Panic and Agoraphobia*. London: Academic Press.

HOEKSTRA, R. J., VISSER, S. & EMMELKAMP, P. M. G. (1989) A social learning formulation of the etiology of obsessive-compulsive disorders. In *Annual Series of European Research in Behavior Therapy, Vol. 4: Fresh Perspectives on Anxiety Disorders* (eds P. M. G. Emmelkamp *et al*). Amsterdam: Swets & Zeitlinger.

LEWINSOHN, P. M. & ROSENBAUM, M. (1987) Recall of parental behavior by acute depressives, remitted depressives, and nondepressives. *Journal of Personality and Social Psychology*, **52**, 611–619.

LIEBOWITZ, M. R., GORMAN, J. M., FYER, A. J., *et al* (1985) Social phobia: review of a neglected anxiety disorder. *Archives of General Psychiatry*, **42**, 729–736.

LIOTTI, G. (1986) A model of the cognitive organization in agoraphobia. In *Behavior Therapy: Beyond the Conditioning Framework* (eds P. Eelen & O. Fontaine). Leuven, Belgium: Leuven University Press; Hillsdale, New Jersey: Lawrence Erlbaum Associates.

MARKS, I. M. (1969) *Fears and Phobias*. London: Heinemann.

—— (1987) *Fears, Phobias and Rituals: Panic, Anxiety and their Disorders*. New York: Oxford University Press.

MATHEWS, A. M., GELDER, M. G. & JOHNSTON, D. W. (1981) *Agoraphobia: Nature and Treatment*. London: Tavistock.

PARKER, G. (1979) Reported parental characteristics of agoraphobics and social phobics. *British Journal of Psychiatry*, **135**, 555–560.

—— (1983*a*) *Parental Overprotection: A Risk Factor in Psychosocial Development*. New York: Grune & Stratton.

—— (1983*b*) Parental 'affectionless control' as an antecedent to adult depression. A risk factor delineated. *Archives of General Psychiatry*, **40**, 956–960.

—— (1984) The measurement of pathogenic parental style and its relevance to psychiatric disorder. *Social Psychiatry*, **19**, 75–81.

——, TUPLING, H. & BROWN, L. B. (1979) A parental bonding instrument. *British Journal of Medical Psychology*, **52**, 1–10.

PERRIS, C., JACOBSSON, L., LINDSTRÖM, H., *et al* (1980) Development of a new inventory for assessing memories of parental rearing behaviour. *Acta Psychiatrica Scandinavica*, **61**, 265–274.

——, ARRINDELL, W. A., PERRIS, H., *et al* (1986) Perceived depriving parental rearing and depression. *British Journal of Psychiatry*, **148**, 170–175.

PERSSON, G. & NORDLUND, C. L. (1985) Agoraphobics and social phobics: differences in background factors, syndrome profiles and therapeutic response. *Acta Psychiatrica Scandinavica*, **71**, 148–159.

——, ALSTRÖM, J. E. & NORDLUND, C. L. (1984) Prognostic factors with four treatment methods for phobic disorders. *Acta Psychiatrica Scandinavica*, **69**, 307–318.

RICHMAN, J. A. & FLAHERTY, J. A. (1987) Adult psychosocial assets and depressive mood over time: effects of internalized childhood attachments. *The Journal of Nervous and Mental Disease*, **175**, 703–712.

ROLLINS, B. C. & THOMAS, D. L. (1979) Parental support, power, and control techniques in the socialization of children. In *Contemporary Theories About the Family: Research-Based Theories, Volume I* (eds W. R. Burr, R. Hill, F. I. Nye *et al*). New York: The Free Press.

ROSENTHAL, I. (1963) Reliability of retrospective reports of adolescence. *Journal of Consulting Psychology*, **27**, 189–198.

SHAFAR, S. (1976) Aspects of phobic illness – a study of 90 personal cases. *British Journal of Medical Psychology*, **49**, 221–236.

SNAITH, R. P. (1968) A clinical investigation of phobias. *British Journal of Psychiatry*, **114**, 673–697.

SOLYOM, L., LEDWIDGE, B. & SOLYOM, C. (1986) Delineating social phobia. *British Journal of Psychiatry*, **149**, 464–470.

——, SILBERFELD, M. & SOLYOM, C. (1976) Maternal overprotection in the etiology of agoraphobia. *Canadian Psychiatric Association Journal*, **21**, 109–113.

TEARNAN, B. H., TELCH, M. J. & KEEFE, P. (1984) Etiology and onset of agoraphobia: a critical review. *Comprehensive Psychiatry*, **25**, 51–62.

TEEVAN, R. C. & MCGHEE, P. E. (1972) Childhood development of fear of failure motivation. *Journal of Personality and Social Psychology*, **21**, 345–348.

THYER, B. A., NESSE, R. M., CAMERON, O. G., *et al* (1985) Agoraphobia: a test of the separation anxiety hypothesis. *Behaviour Research and Therapy*, **23**, 75–78.

TUCKER, W. I. (1956) Diagnosis and treatment of the phobic reaction. *American Journal of Psychiatry*, **112**, 825–830.

WEBSTER, A. S. (1953) The development of phobias in married women. *Psychological Monographs: General and Applied*, **67**, 1–18.

WOLFE, B. E. (1984) Gender ideology and phobias in women. In *Sex Roles and Psychopathology* (ed. C. S. Widom). New York: Plenum Press.

WOLKIND, S. & COLEMAN, E. Z. (1983) Adult psychiatric disorder and childhood experiences: the validity of retrospective data. *British Journal of Psychiatry*, **143**, 188–191.

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Point of View

Age at Puberty and Mental Illness
Towards a Neurodevelopmental Aetiology of Kraepelin's Endogenous Psychoses*

LETTEN F. SAUGSTAD

The hypothesis of a neurodevelopmental aetiology of manic–depressive psychosis and schizophrenia is based on the relation between onset of puberty and the final regressive events in the central nervous system (elimination of 40% of neuronal synapses), and the discrepancy in body build in the two disorders which is similar to that between early- and late-maturing individuals. The marked rise in manic–depressive psychoses and decline in schizophrenia, particularly the non-paranoid categories, accompanying the decline in mean pubertal age by some four years during the past hundred years are taken as evidence that manic–depressive psychosis affects early maturers and schizophrenia particularly affects late maturers. Gender differences and social differentials accord with this theory. Redundancy of neuronal synapses characterises manic–depressive psychosis, and reduced density of synapses is a characteristic of schizophrenia, whereas 'normality', with optimal synaptic density, is in between.

The hypothesis is presented that the aetiology of manic–depressive psychosis (MDP) and schizophrenia is neurodevelopmental, arising from maturational irregularities in the central nervous system (CNS) in individuals with very early and extremely late puberty. This hypothesis is based on the relation between onset of puberty and the last major step in brain development, and the discrepancy in body build in MDP and schizophrenia which is similar to that between very early and extremely late maturing individuals.

In the human species, onset of puberty is considered to coincide with the final regressive event in the CNS (elimination of about 40% of neuronal synapses) (Huttenlocker, 1984; Ribchester, 1986; Goldman-Rakiĉ, 1988: Rakiĉ, 1989). Any irregularity at this stage will alter later brain function; such maturational irregularities are most likely to occur at the extremes of very early or extremely late puberty.

Early maturers (early puberty) tend to be pyknic (stocky), and late maturers tend to be leptosomic (slender) (Marshall & Tanner, 1986). According to Kretschmer (1921), pyknic body build predominated in MDP (90% of cases) and leptosomic in schizophrenia (80% of cases) at a time when only around 20% of the general population was of true pyknic or leptosomic build and mean age at menarche was around 15 years.

Age at puberty is only partly genetically determined. The decline in mean age at menarche from just below 17 years 100 years ago to around 13 years today in Western industrialised countries (Marshall & Tanner, 1986) is usually considered a phenotypic response to improved living conditions. Late maturers (mean + 2 s.d.) now experience menarche at about the same age (15 years) as early maturers (mean minus 2 s.d.) a century ago. Concomitantly, there has been a shift from a predominance of leptosomic–athletic and true leptosomic build to pyknic–athletic and true pyknic build. Following this decline in pubertal age, a significant rise in MDP is expected concomitant with a decline in schizophrenia, if MDP does indeed affect very early maturers and schizophrenia extremely late maturing individuals.

Trends in MDP

The Norwegian National Case Register of Serious Mental Disorder comprises all first admissions to psychiatric hospitals and clinics by diagnosis since 1916 (Ødegård, 1971; Saugstad & Ødegård, 1980, 1983, 1985). First admissions classified MDP or reactive depressive psychosis (ICD–9 category 298.0; World Health Organization, 1978) increased by more than 50% between 1926 and 1965. A majority of the latter is diagnosed MDP on readmission. In addition, an increasing proportion of hospital admissions was being classified as non-psychotic, particularly as depression (300.4), which has increased from less than 5% in the 1940s to above 10% in the '60s and now exceeds 20%. A great number of these patients are involuntarily admitted. Similarly in Denmark, where the Danish National Psychiatric Register covers admissions to psychiatric hospitals and clinics, the studies (Weeke *et al*, 1975; Nielsen & Bjørn-Henriksen, 1979) agree that MDP and depressive psychosis (298.0) occur with increasing frequency. In Iceland, Helgason (1979) in his follow-up study observed a lifetime risk of MDP of 3.34% as against 2.72% in 1947, and there was also a marked increase in depressive psychosis (298.0) and in non-psychotic depression (300.4). In the Lundby study from Sweden (Hagnell *et al*, 1982) of in-patients, out-patients, and untreated cases, the probability of suffering a depression increased significantly in both sexes over the period 1947–72, and the risk was highest among those aged 20–30 years. Similar observations have been made in the USA (Klerman, 1978), where there is an alarming increase of depression.

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Trends in schizophrenia

Almost all cases of schizophrenia were admitted, and the admission rate probably approached 90% during 1921–40, and around 80% in the following 26 years in Norway (Ødegård, 1971; Saugstad & Ødegård, 1980, 1983; Saugstad, 1986). The narrowing of the concept of schizophrenia to a disorder with a necessarily poor prognosis, combined with a rising preference for diagnosing intermediate functional psychosis (ICD-9 297, 298, 299), and postponement of a diagnosis of schizophrenia until readmission complicate an assessment of its decline. However, taking into consideration Kretschmer's observation (1921) that the most severe subgroups of schizophrenics such as the non-paranoid (hebephrenia, catatonia, dementia simplex), were the most markedly leptosomic (dysplastic), suggesting that they represent extremely late maturers, a decline is probably mainly recorded in countries with a narrow concept of schizophrenia, such as Norway, Denmark, and Britain, among others.

In Norway, the lifetime risk of schizophrenia (including paranoid psychosis (297)) decreased in the male sex over 1926–65, and the decline is considerable in recent years, although it is not as marked as the reduction in schizophrenia diagnosed on first admission, which fell from more than 60% in 1926 to 19% in 1965, and to 5.5% in 1977–78 (both sexes together). In Denmark, there was a remarkable decline in first admissions for schizophrenia for both sexes over 1970–84 (Strømgren, 1987). We may question to what extent this reflects a true decline, since, of first admissions in 1972 who received the diagnosis that year or in the following 10 years, only 50% of the male and 40% of the female patients received the diagnosis on first admission (Munk-Jørgensen, 1985). A most remarkable feature was, however, the decreased proportion of resident schizophrenics, particularly women. In Scotland, first-admission rates dropped by as much as 40% between 1969 and 1978 (Eagles & Whalley, 1985), and in England and Wales (Saugstad & Ødegård, 1983) the proportion of schizophrenic first admissions (including paranoid psychosis) decreased slightly over 1970–77 (from 13.5% to 11.3%).

In contrast, the prevalence of schizophrenia is persistently high in poorer populations (e.g. in the Istrian region of Yugoslavia, in certain parts of rural Ireland, the Australian aborigines, the Cree Indians and the Salteaux of Northern Saskatchewan (Crocetti *et al*, 1964, 1971; Roy *et al*, 1971; Warner, 1985)). An excessive prevalence of schizophrenia (and extremely low prevalence of MDP) has repeatedly been observed in an isolated region of northern Sweden, where according to Bøøk (1953), as late as 1949, poverty was widespread and death rates were high. Moreover, Bøøk commented upon the uniformity of the clinical picture (a particular type of catatonia). Similar harsh conditions prevailed in the neighbouring regions of Finland, where the prevalence rates of schizophrenia are similarly elevated (Vaisanen, 1975; Lehtinen & Vaisanen, 1981).

Sex differences in age at onset and incidence of MDP

There is a markedly higher lifetime risk of MDP in women than men in most investigations (by 1.5–2.0 times) (Ødegård, 1972*a*; Strømgren, 1976; Rawnsley, 1982), in agreement with expectation from the hypothesis. Onset of MDP in women is also earlier than in men (maximum age-specific rates 30–40 years v. 40–50 years) (Lundquist, 1945).

Sex differences in age at onset and incidence of schizophrenia

It is usually believed that there is no sex difference in the incidence of schizophrenia, but a higher male incidence has been observed. In the USA, Babigan (1980) found higher male rates, and in Norway over 1926–65, Ødegård (1971) found 19% to 36% higher male admission rates. Higher male admission rates have also been recorded in Denmark (Strømgren, 1987), and in the Third World (Sartorius *et al*, 1986, 1987).

Onset of schizophrenia in men is, as expected, earlier than in women, with a difference in maximum age-specific rates of about ten years (Noreik & Ødegård, 1967; Ødegård, 1971). Earlier onset in men is distinguished by being more insidious, with greater chronic defects, and on the whole a less favourable course (Saugstad & Ødegård, 1980, 1986; Watt *et al*, 1983; Strømgren, 1987; Häfner, 1987).

With an earlier puberty (lower proportion of extremely late maturers) the female sex is 'protected' against schizophrenia with later, more acute onset, and a more favourable course. Being older at onset, there is relatively good preservation of the personality, which at that stage is already mature and fully developed, and female schizophrenics stay a shorter time in hospital, and spend longer out of hospital (Strømgren, 1987). This might explain the decrease of resident schizophrenics since 1953 in Denmark being much more pronounced for women. A more intensive study of the limited population of Bornholm in 1935 and in 1983 revealed a considerably decreased prevalence of female schizophrenics compared with a little-changed prevalence in men (Strømgren, 1987).

Trends in subgroups of schizophrenics

In Norway, over 1977–78, when 5.5% of the total 6255 first admissions were classified as schizophrenic, catatonia was diagnosed in only two women and four men, and dementia simplex and hebephrenia in 11 women and 21 men respectively. Whereas previously there had been a predominance of non-paranoid schizophrenia in the men, non-paranoid and paranoid schizophrenia were now about equally rare. In women paranoid schizophrenia predominated, whereas an equal proportion of non-paranoid and paranoid schizophrenics had been found in previous investigations (Saugstad & Ødegård, 1980).

This decline in the most severe subgroups such as the non-paranoid (hebephrenia, catatonia, dementia simplex) has often been accepted as due to drug treatment. The drugs cannot affect age at onset. The non-paranoid, with their most pronounced leptosomic (dysplastic) body build and particularly early and insidious onset, probably belong to the most extreme categories of late maturers. The marked reduction in these cases is therefore more likely a result of their significant reduction in the population. This is illustrated by the fact that Kretschmer's observation of leptosomic–dysplastic body build (acromegaloidism, eunuchoidism, infantilism, virilism in females, femininity in males, etc.) in 17.5% of schizophrenics (as against 0.4% in MDP) has received no attention lately. It might simply be due to a reduction in the numbers of these cases.

The relation between maturational rate and subgroup of schizophrenia is also illustrated from Asia and Africa, where ethnic groups are more mature throughout growth, with more weight for height than whites, and mature earlier (earlier age at puberty) (Marshall & Tanner, 1986). A greater predominance of paranoid over non-paranoid schizophrenia is observed, and onset is more acute and the course of the disease more favourable, with less chronic defects, than in the European countries included in the WHO study (Sartorius *et al*, 1986, 1987).

Trends in body build

Kretschmer's (1921) observations have been confirmed. There is a persistent discrepancy in body build in MDP and schizophrenia (Langfeldt, 1937). The association is now not so clear, because a rising proportion of cases of schizophrenia are unclassifiable (mixed type) (Astrup *et al*, 1962; Astrup & Noreik, 1966; Price, 1969; Singer, 1972). This has led to the opinion that Kretschmer himself overestimated the strength of the association. With considerably lower mean pubertal age and near disappearance of the extremes of body build in late maturers such as true leptosomic and considerable reduction in leptosomic–athletics, the association between body build and schizophrenia is apt to be less clear. The association has always been most pronounced in males, with puberty on average two years later than in females. The relation between body build and MDP is unaffected. Moreover, when MDP occurs in non-pyknic individuals, the course and prognosis are atypical (Mauz, 1930; Strømgren, 1976). The relation between body build and mental illness has also been confirmed in other ethnic groups (Verghese *et al*, 1978).

Concomitant with the decline in pubertal age, there is an increase in mean adult height of 13 cm and more weight for height. Weight for height has no Gaussian distribution, but the distribution is skewed toward the heavier weights, confirming a change in predominant body build toward the pyknic (stocky) type (Central Bureau of Statistics, 1988).

The social distribution of manic-depressives

Information relating social class to age at puberty is rarely available. A significantly higher rate of MDP in social class I than in the lower social classes has been observed in Finland (Stenbäck & Achté, 1966), in Iceland (Helgason, 1979), and in other countries (Rawnsley, 1982).

In Norway, the social differentials are negligible (Brundtland *et al*, 1980). Ødegård (1963, 1976*b*) followed all students leaving secondary schools in Norway between 1916 and 1929 until 1974, by means of the National Case Register: the female rate for MDP was 2.3 times higher than that in the general population, the male rate 1.7 times higher. The students represented only a few percent ($<5\%$) of the relevant birth cohorts (1895–1910), in largely upper-middle-class families.

The social distribution of schizophrenics

An excess of schizophrenia in the lowest social classes (V) is one of the most consistent and debated findings in psychiatric epidemiology (Ødegård, 1972*b*, 1975*a*). The discrepancy concerns to what extent schizophrenics drift down to or were born and reared in social class V. In America, Hollingshead & Redlich (1958) maintained that the great majority were born and reared there, whereas in Britain Goldberg & Morrison (1963) found that the social distribution of the fathers of schizophrenics equalled that of the general population, and therefore that the schizophrenics drifted down either before or after onset of the disease. The studies are however not comparable, because the British social classification includes only occupation, whereas the Americans used weighted scores for place of residence, level of education, and occupation, which lowers the social class of previous generations. Further, the Americans included mainly chronic in-patients (10–15 years in hospital) adding to a probable social bias towards the lowest socio-economic class. In contrast, the British series could be biased towards the middle classes. This is because only 52% (351/672) of the series drawn by the Registrar General was considered. Among the 321 missing, 163 were excluded because "a large proportion of the patients whose entry could not be found had foreign names and were probably born abroad". The remaining 158 excluded (20–24 years old) were "difficult to interpret, they do not resemble the general population as closely as the fathers of patients aged 25–34 years" (Goldberg & Morrison, 1963). Most likely, therefore, an excess of schizophrenics are born and reared in the lowest socio-economic class, although not a majority (Saugstad, 1989*a*,*b*). The lack of excess of schizophrenics in the lowest class in the Hagerstown study (Clausen & Kohn, 1959) is not convincing. There were several confounding factors, such as the opening of a new private hospital in the middle of the study, with its effect on admission rates, selection of patients, and diagnoses. The number of cases was small, and there was no information on the proportion of single/married, male/female, distribution by occupation, or diagnostic criteria (Saugstad, 1989*a*).

The present minor social differentials in Norway, where no social classification has been constructed that differentiates significantly in mortality, led Ødegård (1975*a*) to use occupations. The total of 34 457 gainfully employed first admissions aged 20–69 years during 1926–50 were divided into 13 occupations. The highest admission rates for schizophrenia were observed in occupations with the lowest standard of training, income and social prestige. More particularly, in these occupations with a decreasing population (farm labourers, seamen) the rates increased in the last decade, whereas they declined in expanding occupations such as technicians.

Discussion

The rise in MDP, including depressive psychosis (ICD–9 298.0) and the decline in schizophrenia, particularly the non-paranoid categories (295.0, 295.1, 295.2), accompanying the significant decline in mean pubertal age in this century, have been taken as evidence suggesting that MDP affects very early maturers and schizophrenia late-maturing individuals, as have the sex differences in incidence and age at onset in MDP and schizophrenia. The different social distribution of MDP and schizophrenia, with an excess of MDP in the highest strata of society and of schizophrenia in the lowest, further strengthens the evidence for a neurodevelopmental aetiology involving maturational irregularities.

A frequent argument to account for the striking rise in depression has been increased social psychological strain. However, the mental disorders most associated with stress and life events are non-psychotic conditions such as the multiple depressive reactions (ICD–9 301.1, 308.1, 308.4, 311, 312, 313, 300.4). It is not usually possible to predict an outbreak of MDP, or relate it to a particular event. The "reactive or psychogenic" depressive psychoses (298.0) are by definition restricted to those which are "largely or entirely attributable to a recent life experience" (ICD–9). In practice, the diagnosis is frequently used without this requirement being fulfilled because of the reluctance to diagnose MDP or schizophrenia on first admission to hospital.

The growing reluctance to diagnose schizophrenia, the predominance of different concepts of the disease, changing diagnostic practice, as well as insufficient information, complicate an assessment of its decline (Saugstad & Ødegård, 1980, 1983, 1985). Furthermore, in countries with high unemployment, a number of schizophrenics are probably living in the community (Wiersma *et al*, 1983), receiving social benefits without ever having had a psychiatric examination. The striking decline in admissions classified as non-paranoid schizophrenia in Norway and Denmark is, however, accepted as reflecting a true decline, which is also illustrated from Denmark in the decrease in schizophrenic in-patients (Strømgren, 1987). There is no information from Britain concerning the decline in schizophrenia by subgroup.

Experienced psychiatrists like Ødegård (1972*a*) and Strømgren (1982) agree that the clinical picture of schizophrenia has changed continuously during the last 40–50 years, and that severe deterioration is now not often seen. We seem to observe an increasing number of acute, latent, schizoaffective and borderline psychotic conditions. These conditions have probably always been included in the concept of schizophrenia in the USA (until the introduction of DSM–III in 1980). They were possibly becoming increasingly frequent. This led Kasanin (1933) to introduce the concept of schizoaffective disorder, Hoch & Polatin (1949) latent or pseudoneurotic schizophrenia, Kety *et al* (1968) the spectrum schizophrenia, and Knight (1954) borderline schizophrenia. Subgroups of schizophrenics had already been described by French and German psychiatrists in the last century or the beginning of this century (Pichot, 1983). The unchanged, high proportion of first admissions classified schizophrenic in the USA in 1969 and 1975 (46.6%), without breakdown by subgroup, is therefore no argument against a decline in the most severe (least treatable) subgroups such as catatonia, hebephrenia and simple schizophrenia.

The non-paranoid schizophrenics with their extreme body build are probably those with the most delayed puberty, whereas puberty is possibly less delayed in paranoid schizophrenia and in subgroups with a favourable prognosis. In view of the relation between mean pubertal age and standard of living, we might speculate that the reason for the early introduction of the concept of intermediate functional psychoses (reactive or psychogenic) in Norway (1911) and Denmark (1916), for clinical conditions which in other countries would have been diagnosed as schizophrenia or MDP, was simply that these clinical pictures were comparatively more frequent because of the comparatively high standard of living (lower mean pubertal age).

Why is schizophrenia of early onset, particularly in the male sex?

A neurodevelopmental aetiology involving maturational irregularities in the CNS in extremely late-maturing schizophrenics implies that the attenuation of synaptic density goes beyond the optimal, and reduced synaptic density results. This reduction in density of synapses is invariably most pronounced in males, because of their later puberty. An earlier onset and more severe course is therefore to be expected.

The synapses that die are dispersed among those that survive, and we would therefore expect only subtle, unspecific structural cerebral deficits. Because regions of the neocortex, particularly the anterior and superior frontal cortex, are probably the last to reach adult levels of synaptic density (Rakić, 1989; Phelps *et al*, 1989), maximum reduction in density of synapses is expected in these regions. Verification of brain pathology specific to schizophrenia has not been easy. There is invariably considerable overlap between schizophrenics and controls. Several studies have had to rely on statistical comparisons of means in order to observe differences. However, there is agreement that the brain in schizophrenia is structurally abnormal. It manifests, in accordance with expectation, a condition of subtle structural deficits, often with a frontocortical maximum (Andreasen *et al*, 1982; Shelton & Weinberger, 1986). When cerebral atrophy is found, there is a high frequency of pre- and peri-natal morbidity (Shelton & Weinberger, 1986).

Clinically, it seems reasonable to consider the dependency of schizophrenics on their social environment (inability to choose their own suitable environment), because of their excessive vulnerability to overstimulation (high expressed emotions, noisome occupations, etc.) as well as to understimulation (social isolation), as reflecting their neurodevelopmental disorder. The detrimental effect of low IQ on the course and prognosis of the disease (Jones & Offord, 1975) is also in accord with the hypothesis if the neurodevelopmental disorder has this particular characteristic.

Why does MDP occur at any age, and particularly in females?

A certain shortening of the pre-pubertal growth period is probably accompanied by higher rates of elimination of synapses. In very early maturing MDP with a marked reduction in this final stage of brain reorganisation, irregularities and insufficient elimination of synapses could occur. It is suggested that incomplete final adjustment and a persistency of supernumerary synapses characterise MDP. The redundancy is most pronounced in the female sex with an earlier average puberty, and MDP is also more common. A redundancy of synapses is not verifiable, even with our refined neuroradiological methods. The reports of "no definite pathological changes in the CNS" in the main group of MDP (Ashcroft, 1982) is therefore in agreement with expectation, as is the return of the personality to normal between the psychotic episodes. A psychotic breakdown can occur at any age, in the young (under 20 years) as well as in the old (over 70 years) (Stenstedt, 1952; Helgason, 1979), but the maximum age-specific rate is about 10 years earlier in women.

The insufficiency of genetics in MDP

The suggestion that MDP might be 'caused' by a single heterozygous genotype on chromosome 11 (Egeland *et al*, 1987), or in some cases by an allele on the X chromosome (Baron *et al*, 1987), is not contrary to the view that very early puberty is the necessary factor for the development of MDP. The allele by itself is not necessarily causative: less than 70% of those who inherit the allele develop the disorder.

The insufficiency of genetics in schizophrenia

Although a genetic aetiology for schizophrenia is highly convincing in studies of multiplex families, the low proportion of such multiply affected families and the great number of sporadic cases underline the uncertainty about a genetic component. The high discordance rate (>50%) in monozygotic twins stresses the insufficiency of a genetic factor. We (Saugstad & Ødegård, 1986*a*) were unable to demonstrate any significant correlation between inbreeding in rural communities in Norway in 1891 (mean 8.3%, range 4–31%) and first-admission rates to psychiatric hospitals over 1921–40 (>80% schizophrenic). Psychiatric morbidity as measured by first admission to psychiatric hospitals in Norway over 1926–55 (22 000 admissions) was also lower than expected among offspring of consanguineous parentage in comparison with the general population. In Helgason's (1979) investigation of all first-cousin marriages in Iceland during 1916–64, only the rates of mental retardation and organic syndromes were higher than in the controls.

Sherrington *et al* (1988) suggested a susceptibility locus for schizophrenia on chromosome 5. However, Kennedy *et al* (1988), in their investigation of the genetically homogeneous population of the isolated region in Northern Sweden (Bøøk, 1953), have produced strong evidence against such linkage. This is of particular interest since the population in question was traced back to three Finnish families settling in the region. The authors commented upon the predominance of severe subgroups of schizophrenia, in accordance with Bøøk's description from 1953. In this particular region where harsh conditions prevailed as late as 1949, mean pubertal age was probably well above the mean for Sweden, and the proportion of late-maturers considerably increased. Very late puberty as the necessary factor for the development of schizophrenia with its high prevalence in this area is clearly supported.

MDP and schizophrenia have existed as long as mankind

If MDP and schizophrenia are caused by maturational irregularities in the CNS of those maturing very early and extremely late respectively, then Kraepelin's endogenous psychoses have probably existed as long as mankind. Improvements in living conditions, which increase rate of maturation, increase the incidence of early maturers and thereby that of MDP, concomitantly with a decrease in late maturers and schizophrenia.

With this relation between standard of living, age at puberty, and the two mental disorders, the question arises as to whether standard of living in the last century in Europe was a recent achievement or of longer duration. That is to say, was the incidence of schizophrenia declining or stable? In Norway, with its late industrial revolution (latter half of the last century), a decline in living standard was prevented by massive overseas migration (second only to Ireland) (Saugstad, 1979). The living conditions in the above-mentioned northern Swedish area were probably not much different from those in Norway, and we would therefore imagine a similarly high prevalance of schizophrenia and an extremely low prevalence of MDP. This cannot be confirmed, despite the fact that Norwegian admission statistics go back to 1850. Attempts to conceptualise schizophrenia were first developed in the latter half of the century. Moreover, depressions were explicitly excluded from the census on insanity in 1835. In Norway as well as in England, the last century and the beginning of this were devoted to the immense social task of building mental hospitals. With inadequate hospital facilities, the most severe cases and new cases of schizophrenia were selected for admission. The last century was also a period of therapeutic optimism (moral treatment), an attitude which was essential in filling up the new hospitals, but which prevents any estimate of secular changes.

Anorexia nervosa – a disorder of early maturation?

The effect of gender and social class on maturational rate makes it reasonable to ask whether there are other disorders, more common in the female sex and upper-middle classes, and increasing in the population, in which early maturation could be involved. Anorexia nervosa and bulimia nervosa affect the female sex in particular and the upper-middle classes (Russel, 1983). They are steadily increasing, and they affect maturational rate. Moreover, there is clinical and experimental evidence of hypothalamic dysfunction in these disorders. There are also reports of the coexistence of MDP in some cases, and lithium has sometimes proved a successful treatment (Cantwell *et al*, 1977; Stein *et al*, 1982; De Vries, 1985).

No continuum of psychosis from MDP to schizophrenia

A continuum of psychosis from MDP to schizophrenia is unlikely if we accept a neurodevelopmental aetiology of Kraepelin's endogenous psychoses. This is because normality, with optimal density of synapses, is between the early-maturing MDP, with redundancy of synapses, and the late-maturing schizophrenia, with reduced synaptic density.

Schizophrenic disturbance of thinking is usually readily distinguished from manic–depressive mood swings. They are clearly different and specific psychopathological dimensions. However, the two disorders have also several symptoms in common, and we would expect similar areas and structures of the brain to be involved – those fundamental to emotional and cognitive behaviour (neocortex, limbic system, hypothalamus, etc.).

It seems reasonable to ask how it is possible to explain that a redundancy of synapses can result in excessive mood swings, whereas the attenuation of synaptic density is associated with cognitive defects. The hierarchical order of maturation in the CNS is probably crucial in this connection, because it implies that the sites of change differ in the two disorders. The phylogenetically oldest structures, such as the brainstem, thalamus, hypothalamus, etc., are the first to mature. The neocortex, particularly the anterior and superior part of the frontal cortex, is the last. So only in very early maturers could synaptogenesis be prevented in some of the phylogenetically oldest structures. In contrast we would expect maximum reduction in synaptic density to involve the anterior and superior part of the frontal cortex in late-maturing schizophrenics, such as has repeatedly been observed (Andreasen *et al*, 1982).

Schizophrenia – the final common path

Classic MDP, with its excessive mood swings and return of the normal personality between relapses, is unique: no single similar disease or injury has been identified. When MDP occurs in non-pyknic individuals, the course and prognosis are atypical (Mauz, 1930). In contrast, classic endogenous schizophrenia with its subtle non-specific structural deficits, although the most common, is but one of several schizophrenias. Several diseases (inherited and other) may present as schizophrenia. In these cases there are usually neurological signs and symptoms, and cerebral atrophy is often found (Propping, 1983; Saugstad & Ødegård, 1986*b*). Schizophrenia can also result from an early brain lesion affecting first and/or second regressive event in the CNS (at 4–5 months of pregnancy, or 1–2 years of life), which remains clinically unnoticed until around puberty when it interacts with the developmental regression of excessive interneuronal contacts (the final regressive event in the CNS) leading to the later onset of psychosis. Depending upon the site and extent of the primary lesion and rate of maturation, a variety of psychopathological conditions is observed in these cases, ranging from non-paranoid and paranoid, to the more favourable subgroups of schizophrenia, borderline conditions, and schizoaffective. Sometimes one has the impression of a continuum of psychosis, without, however, the inclusion of classic MDP. Finally, we observe cases of childhood psychoses (childhood schizophrenia, infantile autism) where the primary lesion prenatally and/or perinatally is in itself sufficient to affect early infant behaviour to such an extent. In such cases, onset of puberty is usually accompanied by an increase in EEG abnormalities, grand mal seizures, the mental defect often seems more severe, and a changing psychopathology is often observed which requires a change in medication. Because the early onset basically disturbs development, these psychoses are not directly comparable to adult schizophrenia. However, the characteristic perceptual disturbances, hypo- and hyper-responsiveness to stimuli as well as their fluctuating nature and the detrimental effect of low IQ, are comparable (Saugstad, 1989*a*).

Schizophrenia is therefore a final common path: a brain reaction to a variety of adverse factors acting pre-, peri- and post-natally. In contrast to MDP, personality does not return to normal between the psychotic episodes in schizophrenia. We observe personality change, and a longer stay in hospital is often needed, as well as chronic neuroleptic treatment. A reduction in these cases is therefore particularly desirable. Through our improvement in living conditions in this century, and in particular the reduction in the proportion of very late maturers (late puberty) in the population, we have seen a reduction in the most severe, least treatable forms of the endogenous neurodevelopmental schizophrenia, the non-paranoid. Considering the exogenous schizophrenias, whether with onset in childhood or after puberty, but where a brain lesion pre- and/or perinatally is essential in the development of the disorder, we may ask whether a reduction in the sequelae of pre- and perinatal morbidity is in sight. Factors killing infants at or around birth are similar to those operating in pre- and/or perinatal morbidity (Saugstad, 1981). The significant reduction in infant mortality in this century is therefore probably also reflected in a reduction in the sequelae of pre- and perinatal morbidity. We may therefore already be experiencing a reduction in these schizophrenias with an exogenous aetiology. To gain more insight into these matters, and to enable comparison between different series of schizophrenics from different countries, we need to establish standardised criteria for optimal conditions, pre-, peri- and post-natally (Saugstad, 1981, 1985).

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References

Andreasen, N. C., Nasrallah, H. A., Dunn, V., *et al* (1982) Structural abnormalities in the frontal region in schizophrenia. *Archives of General Psychiatry*, 43, 136–144.

Ashcroft, G. (1982) Biochemistry and pathology of the affective psychoses. In *Handbook of Psychiatry 3: Psychoses of Uncertain Etiology* (eds J. K. Wing and L. Wing), pp. 160–165. Cambridge: Cambridge University Press.

Astrup, C., Fossum, A. & Holmboe, R. (1962) *Prognosis in Functional Psychoses*. Springfield Illinois: Thomas.

—— & Noreik, K. (1966) *Functional Psychoses*. Springfield Illinois: Thomas.

Babigan, H. M. (1980) Schizophrenia. Epidemiology. In *Comprehensive Textbook of Psychiatry, III* (eds H. I. Kaplan, A. M. Freedman and B. J. Sadock), pp. 1121–1131. Baltimore: Williams & Wilkins.

Baron, M. N., Risch, R., Hamburger, B., *et al* (1987) Genetic linkage between X-chromosome markers and bipolar affective illness. *Nature*, **326**, 289–292.

Bøøk, J. A. (1953) A genetic and neuropsychiatric investigation of a North Swedish population. *Acta Genetica (Basel)*, 4, 1–100.

Brundtland, G. H., Liestøl, K. & Walløe, L. (1980) Height, weight and menarcheal age of Oslo school children during the last 60 years. *Annals of Human Biology*, 7, 307–322.

Cantwell, D. P., Sturzenberg, S., Buttoughs, J., *et al* (1977) Anorexia nervosa, an affective disorder. *Archives of General Psychiatry*, **34**, 1087–1093.

Central Bureau of Statistics (1988) *Yearbook 1988*. Oslo: Central Bureau of Statistics.

Clausen, J. A. & Kohn, M. L. (1959) Schizophrenia and the social structure. In *Epidemiology of Mental Disorder*, Publication 60 (ed. B. Pasamanick), pp. 69–94. Washington, DC: American Association for the Advancement of Science.

Crocetti, G. M., Kulcar, Z., Kesic, B., *et al* (1964) Differential rates of schizophrenia in Croatia, Yugoslavia. *American Journal of Public Health*, **54**, 196–206.

——, Lemkau, P. V., Kulcar, Z., *et al* (1971) Selected aspects of the epidemiology of psychoses in Croatia, Yugoslavia. *American Journal of Epidemiology*, **94**, 126–134.

De Vries, M. (1985) Anorexia nervosa and affective disorder. *American Journal of Psychiatry*, **142**, 1–2.

Eagles, J. K. & Whalley, L. J. (1985) Decline in the diagnosis of schizophrenia among first admissions to Scottish mental hospitals from 1969–78. *British Journal of Psychiatry*, **146**, 151–54.

Egeland, J. A., Gerhardt, D. S., Pauls, D. L., *et al* (1987) Bipolar affective disorder linked to DNA markers on chromosome 11. *Nature*, **325**, 783–787.

Goldberg, E. M. & Morrison, S. L. (1963) Schizophrenia and social class. *British Journal of Psychiatry*, **109**, 785–802.

Goldman-Rakič, P. S. (1989) Development of cortical circuity. *International Wallenberg Symposium on Neurobiology of Early Infant Behaviour. Stockholm: 28 August–1 September 1988.* New York: Plenum.

Häfner, H. (1987) The epidemiology of schizophrenia. In *Search for the Causes of Schizophrenia* (eds H. Häfner, W. F. Gattaz and W. Yanzarik), pp. 47–74. Stuttgart: Springer Verlag.

Hagnell, O., Lanke, J., Rohrsman, B., *et al* (1982) Are we entering an age of melancholy? *Psychological Medicine*, **12**, 279–289.

Helgason, T. (1979) Epidemiological investigations concerning affective disorders. In *Origin, Prevention and Treatment of Affective Disorder* (eds M. Schou & E. Strømgren), pp. 241–255. London: Academic Press.

Hoch, P. H. & Polatin, P. (1949) Pseudoneurotic forms of schizophrenia. *Psychiatric Quarterly*, **23**, 248–276.

Hollingshead, A. B. & Redlich, F. C. (1958) *Social Class and Mental Illness*. New York: John Wiley & Sons.

Huttenlocker, P. R. (1984) Synapses: elimination and plasticity in developing human cerebral cortex. *American Journal of Mental Deficiency*, **88**, 488–496.

Jones, M. B. & Offord, D. R. (1975) Independent transmission of IQ and schizophrenia. *British Journal of Psychiatry*, **126**, 185–190.

Kasanin, J. (1933) The acute schizo-affective psychosis. *American Journal of Psychiatry*, 13, 97–126.

Kennedy, J. L., Gluffra, L. A., Moises, H. W. *et al* (1988) Evidence against linkage of schizophrenia to markers on chromosome 5 in a northern Swedish pedigree. *Nature*, **336**, 167–170.

Kety, S. S., Rosenthal, D., Wender, R., *et al* (1968) The types and prevalence of mental illness in the biological and adoptive families of adopted schizophrenics. In *The Transmission of Schizophrenia* (eds D. Rosenthal & S. S. Kety). New York: Pergamon Press.

Klerman, G. L. (1978) Affective disorders. In *Harvard Guide to Modern Psychiatry* (eds M. Armand & M. D. Nicholi Jr), pp. 253–281. Cambridge, Mass: Belknap Press.

Knight, R. P. (1954) Borderline states. In *Psychoanalytic Psychiatry and Psychology* (eds R. P. Knight & C. R. Freidman). New York: Internal University Press.

Kretschmer, E. (1921) *Kǒrperbau und Charakter*. Heidelberg: Springer Verlag.

Langfeldt, G. (1937) *The Prognosis in Schizophrenia and the Factors influencing the Course of the Disease*. Copenhagen: Munksgård.

Lehtinen, V. & Vaisanen, E. (1981) Epidemiology of psychiatric disorder in Finland. *Social Psychiatry*, 16, 61–180.

Lundquist, G. (1945) Prognosis and course in manic–depressive psychoses. *Acta Psychiatrica Scandinavica* (suppl. 35).

Marshall, W. A. & Tanner, J. M. (1986) Puberty. In *Human Growth*, vol. II (eds F. Falkner & J. M. Tanner, pp. 171–209. New York: Plenum Press.

Mauz, F. (1930) *Die Prognostik der Endogenen Psychosen.* Stuttgart: Thieme Verlag.

Munk-Jørgensen, P. (1985) Decreasing first admission rates of schizophrenia among males in Denmark from 1970 to 1984. *Acta Psychiatrica Scandinavica*, **73**, 645–650.

Nielsen, A. & Bjørn-Henriksen, I (1979) Prevalence and disease expectancy for depressive psychoses. In *Origin, Prevention and Treatment of Affective Disorders* (eds M. Schou & E. Strømgren), pp. 199–206. London: Academic Press.

Noreik, K. & Ødegård, Ø. (1967) Age at onset of schizophrenia in relation to socio-economic factors. *British Journal of Psychiatry*, **124**, 243–249.

Ødegård, Ø. (1963) Mental disease in Norwegians with a high-school background. *Acta Psychiatrica Scandinavica*, **39**, 31–40.

—— (1971) Hospitalized psychoses in Norway. Time-trends in 1926–65. *International Journal of Social Psychiatry*, **6**, 53–58.

—— (1972*a*) The multifactorial theory of the inheritance in predisposition to schizophrenia. In *Genetic Factors in Schizophrenia* (ed. A. R. Kaplan), pp. 256–295. Springfield, Illinois: Thomas.

—— (1972*b*) The epidemiology of the psychoses. In *Psychiatrie der Gegenwart*, band II, teil 1 (eds K. P. Kisker, J.-E. Meyer, M. Müller & E. Strømgren), pp. 213–258. Heidelberg: Springer Verlag.

—— (1975*a*) Social and ecological factors in the etiology, outcome, treatment and prevention of mental disorders. In *Psychiatrie der Gegenwart*, band III (eds K. P. Kisker, J.-E. Meyer & E. Strømgren), pp. 151–198. Heidelberg: Springer Verlag.

—— (1975*b*) Morbidity and social mobility in an upper class educational group. *Acta Psychiatrica Scandinavica*, **52**, 36–48.

Phelps, M., Chugani, H. T. & Mazziotta, J. C. (1989) Metabolic assessment of functional maturation and neuronal plasticity of the human brain. In *International Wallenberg Symposium on Neurobiology of Early Infant Behaviour. Stockholm: August 28–September 1, 1988.* New York: Plenum Press.

Pichot, P. J. (1983) *A Century of Psychiatry*. Paris: Roger Dacosta.

Price, J. (1969) An anthropometic comparison of psychiatric patients and their siblings. *British Journal of Psychiatry*, **115**, 435–442.

Propping, P. (1983) Genetic disorders presenting as "schizophrenia". *Human Genetics*, **65**, 1–10.

Rakić, P. (1989) Development of the primate visual pathway. *International Wallenburg Symposium on Neurobiology of Early Infant Behaviour, Stockholm August 28–September 1, 1988.* New York: Plenum Press.

Rawnsley, K. (1982) Epidemiology of affective psychoses. In *Handbook of Psychiatry 3, Psychoses of Uncertain Etiology* (eds J. K. Wing & L. Wing), pp. 134–140. Cambridge: Cambridge University Press.

Ribchester, R. R. (1986) *Molecule, Nerve and Embryo*. Glasgow: Blackwell.

Roy, C., Choudhure, A. & Irvine, D. (1971) The prevalence of mental disorders among Saskatchewan Indians. *Journal of Cross-Cultural Psychology*, **1**, 383–392.

Russel, G. F. M. (1983) Anorexia nervosa and bulimia nervosa. In *Handbook of Psychiatry 4: The Neuroses and Personality Disorders* (eds G. F. M. Russel & L. A. Hersov), pp. 285–297. Cambridge: Cambridge University Press.

Sartorius, N., Jablensky, A., Korten, A., *et al* (1986) Early manifestations and first-contact incidence of schizophrenia in different cultures. *Psychological Medicine*, **16**, 909–928.

——, ——, Ernberg, G., *et al* (1987) Course of schizophrenia in different countries. Some results of a WHO international comparative 5-year follow-up study. In *Search for the Causes of Schizophrenia* (eds H. Häfner, W. F. Gattaz & W. Janzarik), pp. 107–113. Berlin: Springer Verlag.

Saugstad, L. F. (1979) Crude death and infant mortality 1840–1900 in Norway, Sweden, Denmark and England & Wales. *Scandinavian Population Studies*, **5**, 83–97.

—— (1981) Weight of all births and infant mortality. *Journal of Epidemiology and Community Health*, **35**, 185–191.

—— (1985) The relation between nature and nurture in mental subnormality. *Nordisk Psykiatrisk Tidsskrift*, **39**, 85–94.

—— (1986) An example from the Norwegian register. In *Psychiatric Case Registers in Public Health* (eds G. T. ten Horn, R. Giel, W. Gulbinat & J. H. Henderson), pp. 44–60. Amsterdam: Elsevier.

—— (1989*a*) Social class, marriage and fertility in schizophrenia. *Schizophrenia Bulletin*, **15**, 9–43.

—— (1989*b*) Mental illness and cognition in relation to age at puberty. *Clinical Genetics*, **35**, 1–12.

—— & Ødegård, Ø. (1980) Ingen internasjonal tilnaerming. *Nordisk Psykiatrisk Tidsskrift*, **34**, 455–464.

—— & —— (1983) Persistent discrepancy in international diagnostic practice since 1970. *Acta Psychiatrica Scandinavica*, **68**, 501–510.

—— & —— (1985) In defence of international classification. *Psychological Medicine*, **15**, 1–2.

—— & —— (1986*a*) Inbreeding and schizophrenia. *Clinical Genetics*, **39**, 261–271.

—— & —— (1986*b*) Huntington's chorea in Norway. *Psychological Medicine*, **16**, 39–48.

—— & —— (1987) Inbreeding and the epidemiology of schizophrenia. In *Human Genetics* (eds F. Vogel & K. Sperling), pp. 466–473. Berlin: Springer Verlag.

Shelton, K. & Weinberger, D. R. (1986) X-ray computerized tomography studies in schizophrenia. In *Handbook of Schizophrenia* vol. I. (eds H. A. Nasrallah & D. R. Weinberger), pp. 207–250. Amsterdam: Elsevier.

Sherrington, R., Brynjolfsson, J., Petursson, H. *et al* (1988) Localization of a susceptibility locus for schizophrenia on chromosome 5. *Nature*, **336**, 164–167.

Singer, K. (1972) Physique, personality and mental illness in the southern Chinese. *British Journal of Psychiatry*, **121**, 315–319.

Stein, G. S., Hartshorn, J., Jones, J., *et al* (1982) Lithium in a case of severe anorexia nervosa. *British Journal of Psychiatry*, **140**, 526–528.

Stenbäck, A. & Achté, K. A. (1966) Hospital first-admissions and social class. *Acta Psychiatrica Scandinavica*, **42**, 113–125.

Stenstedt, A. (1952) A study in manic–depressive psychosis. *Acta Psychiatrica et Neurologica Scandinavica* (suppl. 79).

Strømgren, E. (1976) *Psykiatri* (12th edn). Copenhagen: Munksgård.

—— (1982) Development of concepts of schizophrenia, subclassification of schizophrenia. In *Handbook of Psychiatry 3, Psychoses of Uncertain Etiology* (eds J. K. Wing & L. Wing), pp. 3–7, 13–16, 28–32. Cambridge: Cambridge University Press.

—— (1987) Changes in the incidence of schizophrenia? *British Journal of Psychiatry*, **150**, 1–7.

Vaisanen, E. (1975) Psychiatric disorders in Finland. *Acta Psychiatrica Scandinavica* (suppl. 263), 22–33.

Verghese, A., Large, P. & Chiu, E. (1978) Relationship between body build and mental illness. *British Journal of Psychiatry*, **132**, 12–15.

Warner, R. (1985) Recovery from schizophrenia. *Psychiatry and Political Economy*, p. 380. London: Routledge & Kegan Paul.

Watt, D. C., Katz, K. & Shepherd, M. (1983) The natural history of schizophrenia. *Psychological Medicine*, **13**, 663–670.

Weeke, A., Bille, M., Videbech, T., *et al* (1975) Incidence of depressive symptoms in a Danish county. *Acta Psychiatrica Scandinavica*, **51**, 28–41.

Wiersma, R., Giel, R., De Jong, A., *et al* (1983) Social class and schizophrenia in a Dutch cohort. *Psychological Medicine*, **13**, 141–150.

World Health Organization (1978) *Mental Disorders. Glossary and Guide to Their Classification in Accordance with the Ninth Revision of the International Classification of Disease* (ICD-9). Geneva: WHO.

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The Evaluation of Psychiatric Illness in Asian Patients by the Hospital Anxiety Depression Scale*

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Twenty Asian psychiatric patients suffering from neurotic illness completed the Urdu version of the HAD Scale. The results were compared with the Clinical Interview Schedule. Somatic symptoms were significantly related to various measures of anxiety but not to those of depression. This finding contradicts the previously held view of linking somatic symptoms with the presentation of depression.

The rapid growth of transcultural psychiatry in the last decade has brought attention to bear on two important points: firstly, that rates of psychiatric morbidity are usually similar in non-Western and Western countries; and secondly, that there are differences in the clinical presentation of various illnesses in different cultures (German, 1987; London, 1988). It has been repeatedly stated that patients of Asian origin tend to express depression in somatic terms (*inter alia* Teja *et al*, 1971; Rack, 1982; London, 1988). Other authors (*inter alia* Rao, 1986) disagree with this notion. In reviewing somatisation, Kirmayer (1984) suggested seven possible categories of aetiological factors. These range from socio-cultural to personal reasons, and include the possible role of the organisation of health-care systems. Many of these factors might be expected to be found in immigrant populations from a different culture.

The aim of the present study was to determine the usefulness of a self-assessment scale, the Hospital Anxiety Depression (HAD) Scale (Zigmond & Snaith, 1983) in Asian patients, and also to study the expression of various psychological and somatic symptoms.

Method

The HAD Scale was translated with the help of seven bilingual collaborators, using the back-translation method (Brislin *et al*, 1973). The Clinical Interview Schedule (CIS; Goldberg *et al*, 1970) was not formally translated, but with the assistance of a group of collaborators the main phrases were translated and every effort was made to keep a constant line of questioning during the interview.

Over a period of 12 months, literate, Urdu-speaking Asian out-patients over 16 years of age who attended the Transcultural (Psychiatric) Clinic at Lynfield Mount Hospital, Bradford, were selected. Patients with organic illness or psychotic symptoms were excluded from the study.

After recording demographic data, all the patients were asked to complete the Urdu version of the HAD Scale. This is a 14-item self-rating scale which presents two subscales, one for depression, one for anxiety. It is claimed that the scale can differentiate between anxiety and depression. Since the scale was designed for use with physically ill patients, the influence of somatic factors has been kept to a minimum. The CIS was then administered (blind to the ratings of the HAD) to the patients by the author, who is a bilingual psychiatrist trained in the procedure. The CIS consists of 10 reported symptoms (anxiety, depression, somatic symptoms, etc.) and 12 manifest abnormalities. Each item is rated on a five-point scale.

Although the HAD was designed to detect a possible case (cut-off 7/8) or a probable case (cut-off 10/11) for each of the two scales, the present study compared the cut-off score of 7/8 with a CIS score of 2 or above on each symptom rating for case identification.

Results

The sample consisted of 9 men and 11 women (mean age 38.7 years, range 25–58 years). Eighteen were married and all were semi-skilled workers who had had some formal education. The mean duration of their symptoms was 4.7 years.

Correlation coefficients were calculated between the somatic symptoms rating on the CIS, and the anxiety and depression scores derived from the HAD and CIS ratings. These showed that there was a statistically significant relationship between the ratings of somatic symptoms and the anxiety scores on the HAD and the CIS. However, the ratings of depression on both these scales failed to show any significant relationship with the CIS item of somatic symptoms (Table I).

In order to evaluate the usefulness of the HAD as a screening instrument for Asian psychiatric patients, the anxiety and depression subscales of the HAD were compared with the CIS anxiety and depression ratings. In

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*Part of the dissertation submitted to the University of Leeds for the degree of MMedSc(Psych). A copy of the Urdu version of the HAD Scale is available from the author.

TABLE I
Correlation coefficient between somatic symptoms and anxiety/depression ratings

Correlation of the CIS somatic symptoms with ratings of	*Pearson's* γ	*Significance*
Anxiety (CIS)	+0.5347	$P<0.01$
Anxiety (HAD)	+0.7315	$P=0.001$
Depression (CIS)	+0.000	NS
Depression (HAD)	+0.1949	NS

the case of the HAD anxiety subscale, specificity was low at 37.5%; sensitivity was 66%. The HAD depression subscale had a specificity of 70% and a sensitivity of 85%.

Discussion

The finding that somatic symptoms are related to anxiety and not to depressive symptoms does not concur with the expectations of other authors, who have implied that somatisation is an expression of depression (e.g. Teja *et al*, 1971; Gada, 1982; Rack, 1982). However, Rao (1986) disagreed with this view when he compared depressive illness in Indian and Western patients; he wrote:

> "Depressed mood is indeed experienced by Indian patients, and by suitable interrogation it could be brought out. . . . Earlier notions of the predominance of somatic symptoms and the rarity of expressed depressed mood as characteristic of depression in India are not now tenable."

The present author has similar clinical experience with Asian patients: these patients tend to focus their attention more on physical than psychological aspects of their problem unless one directly makes this inquiry. It may be that a tendency to focus attention primarily on somatic symptoms is the only cultural element that can be deduced from the present study. However, this cannot be positively substantiated without studying an ethnically different control group.

When the anxiety and depression subscales of the HAD were correlated with the CIS anxiety and depression ratings, the sensitivity and the specificity of the depression subscale was satisfactory but the anxiety subscale had a low specificity. This could be because somatic symptoms, which could be a manifestation of anxiety, were rated separately from anxiety symptoms in the CIS but the HAD had no such facility. Therefore, all anxiety symptoms (which may include somatic symptoms) were rated under a common heading of anxiety in the HAD. Thus the translated version of the HAD Scale failed to identify patients with anxiety (based on the CIS assessment). On the other hand, the patients were able to express their depressive symptoms reasonably well in the interview as well as in the self-rating questionnaire. This is in contrast with the original work of Zigmond & Snaith (1983).

El Rufaie *et al* (1987) claimed that they were able to validate the Arabic version of the HAD in their study in Saudi patients, but they used clinical diagnosis for this comparison. The findings of the present study could be due to the important additional influence of somatic symptoms or due to a particular feature of the sample, namely the longer duration of symptoms.

An important part of the present study was the translation of both the CIS and the HAD Scale for use with Urdu-speaking psychiatric patients. Three main methods for the standard translation of psychometric instruments are discussed by Brislin *et al* (1973). Werner & Campbell (1970) suggested that the back-translation method is the best. The HAD was translated with the help of seven bilingual collaborators, using the back-translation method. The translated version of the Present State Examination (PSE) has been used by Orley & Wing (1979) successfully in Africa. In the International Pilot Study of Schizophrenia (World Health Organization, 1973) the PSE was translated from English into seven languages, and Ben-Tovim (1985) has used the translated version of DSM-III in Botswana. These authors have emphasised the importance of the translation of the concept rather than the literal translation of sentences. The HAD was translated on this principle, and it was surprising to note that a colloquial phrase like "butterflies in the stomach" did not pose a major problem in translation.

As the study involved completing a self-rating scale in Urdu, the main problem encountered was the low literacy rate among the Asian population in Bradford. A preliminary language survey of 100 consecutive Asian patients who attended Lynfield Mount Hospital, Bradford, showed that Punjabi was the main language spoken and only 44% of patients spoke Urdu; 48% of patients were literate in their own language, while 23% were literate in English. This was the main reason for the small size of the present sample.

The present study demonstrates that it is possible to detect depressive illness in Asian patients with the help of a translated version of a self-rating scale. The Urdu version of the HAD Scale is designed in such a way that it could be used by a non-Urdu-speaking clinician to detect psychiatric and in particular depressive illness in Urdu-speaking patients. In its present form the translated version has a limited role as a screening instrument for anxiety and, therefore, is not recommended as a diagnostic device. The scale was acceptable to the patients and the majority had no difficulty in completing it.

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References

Ben-Tovim, D. I. (1985) DSM-III in Botswana: a field trial in a developing country. *American Journal of Psychiatry*, **142**, 342–345.

Brislin, R. W., Lonner, W. J. & Thorndike, R. M. (1973) *Cross-Cultural Research Methods*. New York: John Wiley & Sons.

El-Rufaie, O. E. F. A. (1987) Validity study of the Hospital Anxiety Depression Scale among a group of Saudi patients. *British Journal of Psychiatry*, **151**, 687–688.

Gada, M. T. (1982) A cross cultural study of symptomatology of depression – Eastern versus Western patients. *International Journal of Social Psychiatry*, **28**, 195–202.

German, G. A. (1987) Mental health in Africa: the extent of mental health problems in Africa today. *British Journal of Psychiatry*, **151**, 435–439.

Goldberg, D. P., Copper, B., Eastwood, M. R., *et al* (1970) A standardized psychiatric interview for use in community surveys. *British Journal of Preventive and Social Medicine*, **24**, 18–23.

Kirmayer, L. J. (1984) Culture, affect and somatization: part I & II. *Transcultural Psychiatric Research Review*, **21**, 159–187.

London, M. (1988) Mental illness among immigrant minorities in the United Kingdom. *British Journal of Psychiatry*, **149**, 265–273.

Orley, J. & Wing, J. (1979) Psychiatric disorders in two African villages. *Archives of General Psychiatry*, **36**, 513–520.

Rack, P. (1982) *Race, Culture, and Mental Disorder*. London: Tavistock.

Rao, A. V. (1986) Indian and Western psychiatry: a comparison. In *Transcultural Psychiatry* (ed. J. Cox). London: Croom Helm.

Teja, J. S., Narang, R. L. & Aggarwal, A. K. (1971) Depression across culture. *British Journal of Psychiatry*, **119**, 253–260.

Werner, O. & Campbell, D. (1970) Translating, working through interpreters, and the problems of decentering. In *A Handbook of Methods in Cultural Anthropology* (eds R. Naroll & R. Cohen). New York: American Museum of Natural History.

Zigmond, A. S. & Snaith, R. P. (1983) The hospital anxiety and depression scale. *Acta Psychiatrica Scandinavica*, **67**, 361–370.

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Outcome in Unipolar Affective Disorder after Stereotactic Tractotomy

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An evaluation of 15 patients treated by subcaudate stereotactic tractotomy (SST) for treatment-resistant unipolar affective disorder was made for frequency and severity of recurrence of illness. One-third had died by the time of assessment, but none by suicide. Two-thirds of the sample experienced a reduction in the severity of depressive episodes after the operation; only one-third reported a reduction in frequency of episodes.

The operation of subcaudate stereotactic tractotomy (SST) was developed by Geoffrey Knight in 1965 (Knight, 1965). It is considered appropriate for a minority of patients with severe obsessional disorders, unipolar depression or anxiety states, which are unresponsive to other therapies (Bridges *et al*, 1981). Recent evidence suggests that it may also be helpful in patients with bipolar affective disorder (Lovett & Shaw 1987; Poyton *et al*, 1988).

The original studies on outcome for those patients with severe depression, chronic or recurrent, who underwent stereotactic tractotomy were done in the early 1970s (Strom Olsen & Carlisle, 1971; Bridges *et al*, 1973). A later investigation by Goktepe *et al*

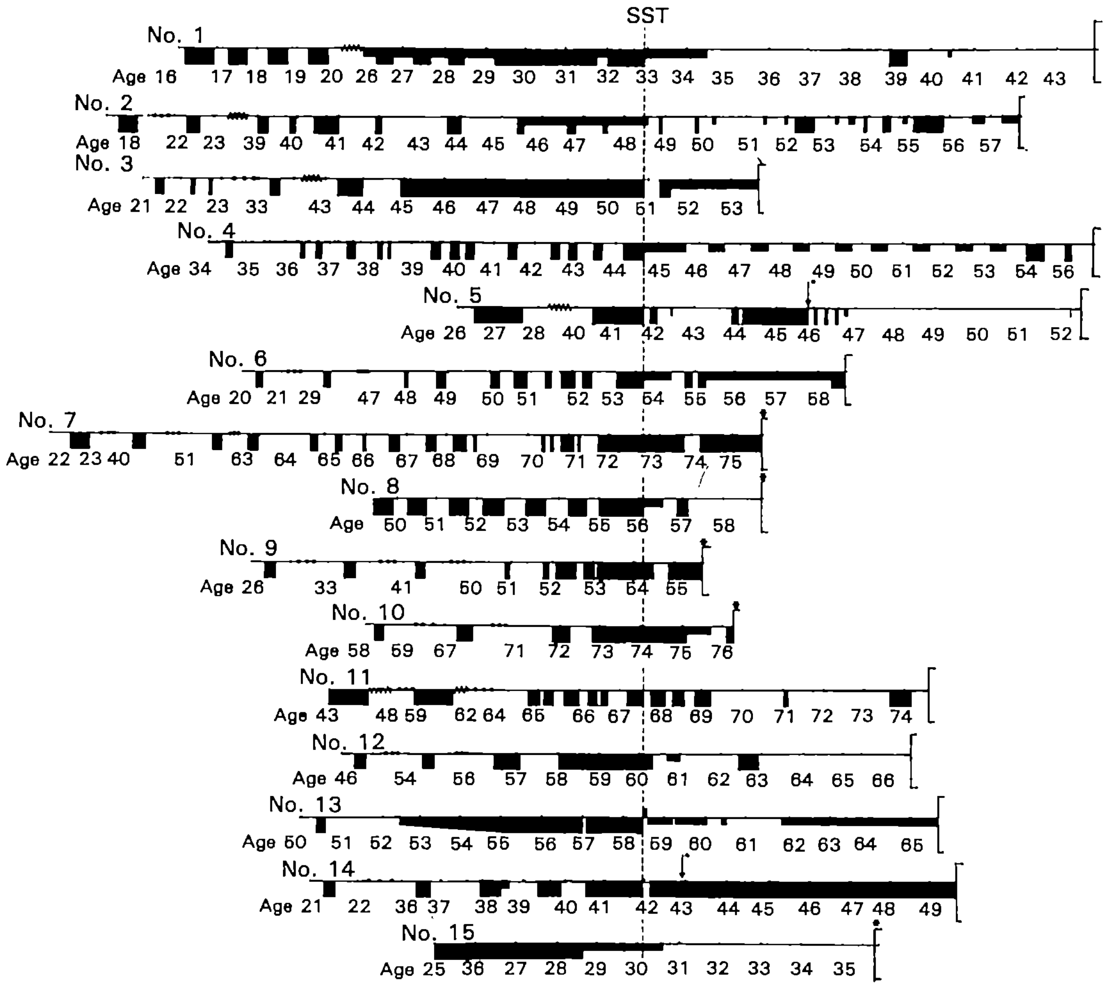

FIG. 1. The time axis is in years and represents the age of the patient. The dotted vertical line marks the point when subcaudate stereotactic tractotomy was performed. An arrow with a star marks an extension. An asterisk marks the time of death. Severe and moderate episodes of illnesses are marked by downward entries; the degree is indicated by the depth of the marker. A squiggly line represents a time collapse when further but poorly documented depressive illness occurred. Dots represent a time collapse which is a known illness-free period.

(1975) reported that almost 60% of those patients suffering from depression had recovered completely or retained only mild symptoms by the time of review, which was between 2½ and 4½ years after surgery. A recent survey of outcome following operation by stereotactic tractotomy or non-stereotactic techniques is reported by Hussain *et al* (1988).

We report on a further 15 cases of patients suffering from unipolar illness who were referred from Whitchurch Hospital, Cardiff, to the Brook Hospital, London, where they underwent SST. The patients had long histories of depressive disturbances in mood which were either recurrent or continuous, and resistant to all treatments available at the time when they were referred. Patients were observed for a mean length of 69 months following the operation (range 16 months to over 10 years), but five had died by the time of assessment. Information on the course of illness was determined by examination of case notes. Interviews, or correspondence, with patients and/or close informants helped to clarify this information and to develop a subjective idea about the outcome of the patients in terms of social functioning and personality change.

Figure 1 shows the pattern of illness for all 15 cases before and after surgery. Entries below the axis represent depressive episodes. We describe one case in detail, chosen for its representative severity of treatment-resistance illness before surgery and moderate outcome following surgery.

Case report

Case one (Figure 1)

The patient came from a high-achieving family and has considerable intelligence. Her mother had a history of depressive illness responsive to monoamine oxidase inhibitors.

The patient's first depressive illness occurred when she was 16 years old and followed a possible mumps encephalitis. There were then three further episodes, each lasting about six months. Although the last of these occurred while she was at university, she completed her degree. During the following six years, she was well enough to complete a higher degree and gain a professional qualification. She worked in her profession for one year before becoming ill again. For the next six years she was continuously ill, with some fluctuation in severity. During some of this time she was employed; however, the jobs were not commensurate with her qualifications. Throughout this time and from adolescence, she suffered from various physical illnesses which included spastic colon, ulcerative colitis, a recurrence of mumps, and glandular fever.

Treatments were numerous and varied during the five years before she underwent stereotactic surgery. When she was 27 she had psychotherapy for one year. She had been receiving nortriptyline for many months, before presenting at Whitchurch Hospital, where she was initially treated with fluanxol and ECT. She was unresponsive to these, and treatment was then attempted with tranylcypromine (40 mg) and lithium. She recovered enough to return to a busy job but rapidly deteriorated. Subsequent treatments included sleep deprivation, tryptophan and prothiaden before she underwent stereotactic surgery when she was 32 years old.

After surgery, her mood improved, but she did not become euthymic until she was prescribed a combination of trimipramine and lithium. Her mood was sustained for four years until treatment with lithium was stopped because of the fear of renal complications. She relapsed into a severe depressive episode which was responsive to ECT. Treatment with lithium was restarted, and for the last two years she has been well, except for one minor episode requiring no change in treatment. She continues to take lithium and a tricyclic antidepressant.

Throughout the last eight years she has had considerable orthopaedic and gynaecological problems. When she was 36 years old she registered as disabled because of back problems, and at the age of 41 she had a hysterectomy and a repair operation for incontinence. Despite these difficulties she has had only the two episodes of depression described above. Although currently unemployed she has worked intermittently over the last eight years. However, she is dissatisfied with her employment record and the fact that she has not managed to live independently of her parents. She is unmarried and has never had a partner. She says that, since surgery, she has become more garrulous and that this has been commented on by friends.

This case is typical in that the treatments given were similar to those received by other patients in the series. All had at least three different antidepressants before SST, which included a monoamine oxidase inhibitor, and many were at some point receiving triple therapy (lithium, monoamine reuptake inhibitor and tryptophan). Following surgery, most have continued on an antidepressant, and in some cases lithium or carbamazepine has been added. The less successful cases have continued to receive a range of treatments similar to that given before SST.

Discussion

This study obviously has a number of limitations. Data collection is retrospective and relies in part on case notes, and the sample size is small. There are no objective baseline data on level of social functioning before SST, and there is no control group. Controversy exists on the natural course of affective disorder (Angst, 1981; Bland, 1985), which means that statements about the progress of each patient's illness pattern with time must be tentative, and changes could be due to chance variations in vulnerability to illness.

With these reservations in mind, the following tentative conclusions may be drawn about the course of unipolar affective disorder following SST:

(a) Two-thirds of the patients experienced some reduction in severity of episodes of illness.
(b) One-third of the patients experienced a reduction in frequency of episodes of illness, and one experienced a reduction in severity as well.
(c) For some patients (cases 5, 10, 11 and 15) drugs which were ineffective before surgery have become effective following surgery. One user (case 15) required no medication at all following surgery, and did well.
(d) One-third of the sample had died by the time of the follow-up (ages 75, 58, 55, 76, 35), none, as far as can be ascertained, by suicide. Four of the patients died because of respiratory or cardiovascular failures.

Thus, although there appears to be attenuation of mood disorder following SST, this improvement is not as impressive as that seen in a series of bipolar patients, all of whom reported a reduction in both severity and frequency of episodes of illness (Lovett & Shaw, 1987). In that study the data suggested that hypomanic episodes of illness were more responsive to SST than depressive episodes, in that they either stopped or occurred in a very much milder form. It could be that depressive episodes in general, but those in unipolar depressive affective disorder in particular, are less sensitive to SST. Another possible explanation for this apparent difference in response to SST could be that unipolar patients underwent the operation at a later stage of illness than did bipolar patients, and consequently are a more treatment-resistant population because they have experienced longer periods of illness and secondary psychosocial deterioration. However, the mean number of years from first episode of illness to SST was approximately 19 years in both groups.

There is little information on whether bipolar and unipolar patients differ in their susceptibility to psychosocial damage inflicted by such prolonged periods of mental illness. If unipolar patients were more vulnerable than bipolar patients to personality deterioration or to the activation of pre-existing personality traits (Kraines, 1957), this could lead to more chronicity of symptoms, dependency and disinclination to relinquish the role of patient. In fact, about half the patients in this series were not functioning well socially and one-third may have suffered deterioration in personality; in some, pre-existing personality traits had caused problems in social adjustment. We base this assessment on careful examination of the case notes and direct reports from patients and close informants. However, assessment of personality in the presence of continuing illness is extremely difficult, and conclusions about this area have to be tentative.

A further explanation for the less-good outcome in this group of patients could be that some suffered from developing and/or undiagnosed pre-existing organic brain disease which altered their response to SST, and the presence of possible brain damage was not considered a contraindication to operation. In the bipolar series, one patient whose course of illness was particularly poor had had embolic cerebral damage before and after the operation, and had an indifferent result. The evidence in these unipolar patients is inconclusive. A patient (case 10) who died of a subarachnoid haemorrhage experienced a course of illness which was unaffected by SST; a CAT scan performed prior to SST showed cortical atrophy. However, a patient (case 8) who was diagnosed as having an Alzheimer's dementia one year after SST experienced a considerable improvement in mood. The prognostic value of diagnosing organic brain disease in assessing outcome following SST has yet to be clarified and should be an area for future study with the more sensitive techniques now available.

References

Angst, J. (1981) Clinical indications for prophylactic treatment of depressions. *Advances in Biological Psychiatry*, **1**, 218–214.

Bartlett, J. R., Bridges, P. K. & Kelly, D. (1981) Contemporary indication for psychosurgery. *British Journal of Psychiatry*, **38**, 507–511.

Bland, R. C. (1985) Clinical features of affective disorders: (a) Diagnosis, classification, rating scales, outcome and epidemiology. In *Pharmacology of Affective Disorders, Theory and Practice* (eds W. G. Dewhurst & G. B. Baker). Durer, New Hampshire: Croom Helm.

Bridges, P. K., Goktepe, E. O. & Maratos, J. (1973) A comparable review of patients with obsessional neurosis and with depression treated with psychosurgery. *British Journal of Psychiatry*, **123**, 663–674.

Goktepe, E. O., Young, L. B. & Bridges, P. K. (1975) A further review of the results of stereotactic subcaudate tractotomy. *British Journal of Psychiatry*, **126**, 270–280.

Hussain, E. S., Freeman, H. & Jones, R. A. (1988) A cohort study of psychosurgery cases from a defined population. *Journal of Neurology, Neurosurgery and Psychiatry*, **51**, 345–352.

Knight, G. D. (1965) Stereotactic tractotomy in the surgical treatment of mental illness. *Journal of Neurology, Neurosurgery and Psychiatry*, **28**, 304–310.

Kraines, S. H. (1957) *Mental Depressions and their Treatment*. New York: MacMillan.

Lovett, L. M. & Shaw, D. M. (1987) Outcome in bipolar affective disorder after stereotactic tractotomy. *British Journal of Psychiatry*, **151**, 113–116.

Strom Olsen, R. & Carlisle, S. (1971) Bifrontal stereotactic tractotomy. *British Journal of Psychiatry*, **118**, 141–154.

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Familial Association of Albinism and Schizophrenia

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Of three siblings in a family, one brother and one sister have both tyrosinase-negative oculocutaneous albinism and a psychotic disorder indistinguishable from schizophrenia. The two disorders may associate within families through genetic linkage or a failure of neurotransmitter homoeostasis.

There have been few descriptions of psychiatric conditions associated with albinism. Case reports include an 11-year-old girl with mild mental retardation and a conduct disorder (Sulestrowska, 1967) and two boys with tyrosinase-positive oculocutaneous albinism (OCA), moderate mental retardation, and autism (Rogawski *et al*, 1978).

The coexistence of albinism and schizophrenic disorders has been presumed to be rare, although single cases have been reported (Arons *et al*, 1968; Leibowitz *et al*, 1978; Pollack & Manschreck, 1986; Clarke, 1987; Jurjus *et al*, 1989). The patient reported by Pollack & Manschreck had tyrosinase-negative OCA and a psychotic disorder meeting DSM–III criteria for schizophrenia; the other authors who described the association in single case reports did not state which type of albinism their patients had, or in most cases their criteria for the diagnosis of schizophrenia. The family reported by Baron (1976) is of particular interest. This study of 22 members of a family of Yemenite-Jewish origin found that five members had both OCA (tyrosinase status not determined) and schizophreniform psychosis (Research Diagnostic Criteria), one non-albino member had schizophrenia, and all other members had neither albinism nor a history of psychotic illness.

We report a family of Irish origin in whom OCA is associated with a psychotic disorder phenomenologically indistinguishable from schizophrenia in two out of three siblings.

Case reports

D, a 39-year-old single, unemployed man, was admitted to hospital after threatening to kill his father. He believed his father was conspiring with other persecutors to thwart D's mission to save mankind. His speech was disordered with illogical shifts in topic and asides such as "thank you for that, Jesus" in response to thought insertion. He was pre-occupied with a complex system of delusions (that he was a member of the SAS with special powers and a mission to marry the reincarnation of "St Theresa the little flower", that he was being watched and persecuted by the CIA and by atheist psychiatrists, that the USSR and USA had joined forces in a plot to invade the UK, and that the IRA had planted bombs under the lawns around the hospital). His attention and concentration were poor because of pre-occupation with delusions. He was correctly orientated. He did not believe he was ill.

Physical examination showed the characteristic features of tyrosinase-negative OCA. Pigment was lacking from his hair, skin, and fundi; his eyes were grey and he had strabismus, nystagmus, and visual impairment. Examination of hair follicles confirmed lack of tyrosinase. A computerised tomography brain scan and 24-hour EEG did not show any abnormality, and examination of chromosomes (with high-resolution banding) was normal. A Present State Examination (Wing *et al*, 1974) carried out as part of another research project found that D's illness fell into CATEGO class S+. The disorder also fulfilled DSM–III–R criteria for schizophrenia (paranoid type) (American Psychiatric Association, 1987).

The psychosis was unusually resistant to neuroleptic drugs, even in high doses, and D's gross delusional state began to resolve only after about five months of treatment. He was discharged home free of delusions nine months after admission, and is at present receiving depot neuroleptics as an out-patient.

D's early life was unremarkable; he attended a Roman Catholic boarding school for the partially sighted between the ages of 5 and 16, and then worked in a warehouse for eight years. He was a shy and introverted man, with few interests other than religion and spectator sports. His history of mental illness dates from the age of 24, when he attended a psychiatric clinic as an out-patient with complaints of depression, insomnia, and "an inferiority complex". He was treated with imipramine, but two months later took an overdose. When assessed by a psychiatrist he described auditory hallucinations, and said he had taken the overdose after hearing God instructing him to do so. He claimed that he was "the son", that his priest was "God", and a friend at work "the Holy Ghost"; and that his Bible and crucifix had been moving around the house of their own accord. A diagnosis of schizophrenia was made, and he was treated with chlorpromazine and subsequently fluphenazine decanoate. His mother said that even with treatment he continued to express delusions of a religious nature (the family are Roman Catholics), and became dull and lacking in spontaneity. In 1974 he complained of low mood and abnormal bodily sensations, and was admitted to hospital and treated with electroconvulsive therapy (ECT) and neuroleptics. Between 1974 and 1986 he continued to live with his parents and attended hospital as an out-patient, receiving flupenthixol decanoate and chlorpromazine. He continued to be pre-occupied with religious delusions. At times he was noted to have formal thought disorder, and he used neologisms ("the rotary as opposed to the sensory component of our bodies" . . . "the trio-conscious"). He has been unemployed since his illness began.

One of his two sisters also suffers from OCA and a similar schizophrenic disorder, the latter diagnosed at the age of 24 years during her third pregnancy. Before this she had an extrovert personality and had been successful both at school and as a mother. She was treated with neuroleptic drugs for about five months with good response, reverting to her usual personality. Unfortunately, she then stopped her medication and for the last 12 years has refused treatment. On recent examination at the age of 36 she was socially isolated, with bizarre behaviour, incongruous affect, and thought disorder. Her illness fulfilled DSM-III-R criteria for schizophrenia (residual type). Her physical stigmata of albinism are identical to those of her brother. Examination of chromosomes with high-resolution banding showed no abnormality.

Both parents are Irish, although from different parts of the country, and there is no question of consanguinity. Neither has albinism nor any history of mental illness. A third sibling is also entirely healthy, and there are no other known cases of either condition in the extended family.

Discussion

Tyrosinase-negative (ty-neg) OCA is the classic type of albinism, in which there is no clinically detectable pigment in skin, hair, or eyes, nor is there evidence of tyrosinase activity in tissues incubated in L-tyrosine or L-dopa. People with ty-neg OCA who come from different racial groups are phenotypically similar, with snow-white hair, pink-white skin with no pigmented naevi, grey to blue irides in tangential illumination, a prominent red reflex from an unmelanised fundus, severe nystagmus and photophobia, and a markedly reduced visual acuity. Ty-neg OCA has a prevalence of 1:39 000 in Caucasians (Witkop *et al*, 1978), although it is more common (about 1:10 000 for all types of albinism) in Northern Ireland (Froggatt, 1960). The lifetime prevalence of schizophrenia is between 1% and 2% (Robins *et al*, 1984), and although higher prevalences have been reported in parts of the Republic of Ireland (Torrey, 1980), a recent study found no markedly increased incidence of schizophrenia (Ni Nuallain *et al*, 1987). Both conditions might be expected to coexist in about 86 people per 370 million of the general population (Pollack & Manschreck, 1986).

The significance of the present report, and that of Baron (1976), lies in the association of these disorders within a family. Such a familial association between albinism and a schizophrenic psychosis might be due to genetic linkage. There is insufficient evidence either in this family or in the literature to substantiate this hypothesis, which would require that a specific genetic locus exists, an allele of which codes for susceptibility to a schizophrenic disorder. A genetic abnormality such as a chromosome deletion or translocation could then affect adjacent loci, and result in both ty-neg OCA and schizophrenic disorder. One report has described a familial association between schizophrenia and a partial trisomy of chromosome 5 (Bassett *et al*, 1988). Another study found genetic linkage of DNA polymorphisms on the long arm of chromosome 5 to schizophrenia, and inferred the existence of a gene locus with a dominant schizophrenia-susceptibility allele which may also predispose to schizophrenia spectrum and other psychiatric disorders (Sherrington *et al*, 1988). A recent report has shown a locus for the human tyrosinase gene on the long arm of chromosome 11 (Barton *et al*, 1988).

Another hypothesis is that a metabolic abnormality associated with albinism produces a predisposition to schizophrenia as a result of disordered neurotransmitter turnover. Tyrosinase is not found in the central nervous system, and it is therefore not possible to postulate a direct effect on cerebral dopaminergic neurotransmission. Baron (1976) suggested that the enhanced retinal photosensitivity of people with albinism might, by altering secretion of melatonin and melanocyte-stimulating hormone, influence mesolimbic and nigrostriatal neurotransmitter homoeostasis, precipitating a schizophrenic disorder. Other workers have suggested a link between disorders of pigmentation and schizophrenic psychoses; Greiner & Nicolson (1965) found hypermelanosis in necropsy material obtained from schizophrenic patients in the period 1947 to 1949, before the introduction of neuroleptics, and suggested that melanosis was a feature of schizophrenia. It is also possible that an association with a schizophrenic disorder could arise because of the disordered neuroanatomy which is known to occur in albinism: abnormalities include an increase in the number of optic neurons crossing to the contralateral side through the optic chiasm (with only the peripheral part of the temporal retina projecting ipsilaterally), and abnormalities in the reticulogeniculate and geniculocortical tracts and cortical visual association areas (Guillery *et al*, 1975; Carroll *et al*, 1980). These abnormalities have been linked to the unusual pattern of cognitive functioning found in children with albinism (Cole *et al*, 1987), and objective abnormalities of visual perceptual ability have been described in association with psychiatric illnesses, including schizophrenia (Flach & Kaplan, 1983).

Other neuroanatomical abnormalities may occur in albinism, and be of significance with regard to the abnormalities of brain lateralisation that have been found to be associated with schizophrenia (Scarone *et al*, 1987).

Our report, together with that of Baron (1976), suggests an association between oculocutaneous albinism and schizophrenic disorders in some families, and has implications for our understanding of the aetiologies of schizophrenic psychoses.

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References

American Psychiatric Association (1987) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn, revised) (DSM-III-R). Washington, DC: APA.

Arons, B., Kosek, J. C. & Forrest, I. S. (1968) Chlorpromazine therapy in a female albino mental patient: clinical, histochemical and biochemical observations. *Life Sciences*, **7**, 1273–1280.

Baron, M. (1976) Albinism and schizophreniform psychosis: a pedigree study. *American Journal of Psychiatry*, **133**, 1070–1073.

Barton, D. E., Kwon, B. S. & Francke, U. (1988) Human tyrosinase gene, mapped to chromosome 11 (q14→q21), defines second region of homology with mouse chromosome 7. *Genomics*, **3**, 17–24.

Bassett, A. S., McGillivray, B. C., Jones, B. D., *et al* (1988) Partial trisomy chromosome 5 cosegregating with schizophrenia. *Lancet*, *i*, 799–801.

Carroll, W. M., Jay, B. S., McDonald, W. I., *et al* (1980) Two distinct patterns of visual evoked response asymmetry in human albinism. *Nature*, **286**, 604–606.

Clarke, D. J. (1987) Paranoid schizophrenia in an Afro-Caribbean albino. *Clinical Notes On-Line*, **2**, 2.

Cole, G. F., Conn, P., Jones, R. B., *et al* (1987) Cognitive functioning in albino children. *Developmental Medicine and Child Neurology*, **29**, 659–665.

Flach, F. F. & Kaplan, M. (1983) Visual perceptual dysfunction in psychiatric patients. *Comprehensive Psychiatry*, **24**, 304–311.

Froggatt, P. (1960) Albinism in Northern Ireland. *Annals of Human Genetics*, **24**, 213–238.

Greiner, A. C. & Nicolson, G. A. (1965) Schizophrenia-melanosis: cause or side effect? *Lancet*, *ii*, 1165–1167.

Guillery, R. W., Okoro, A. N. & Witkop, C. J. (1975) Abnormal visual pathways in the brain of a human albino. *Brain Research*, **96**, 373–377.

Jurjus, G., Moh, P. & Levy, A. B. (1989) Oculocutaneous albinism and schizophrenia-like psychosis. *Journal of Nervous and Mental Disease*, **177**, 112.

Leibowitz, M. R., Dogliotti, M. & Hart, G. (1978) Schizophrenia and albinism. *Dermatologica*, **156**, 367–370.

Ni Nuallain, M., O'Hare, A. & Walsh, D. (1987) Incidence of schizophrenia in Ireland. *Psychological Medicine*, **17**, 943–948.

Pollack, M. H. & Manschreck, T. C. (1986) Oculocutaneous albinism and schizophrenia. *Biological Psychiatry*, **21**, 830–833.

Robins, L. N., Helzer, J. E., Weissman, M. M., *et al* (1984) Lifetime prevalence of specific psychiatric disorders in three sites. *Archives of General Psychiatry*, **41**, 949–958.

Rogawski, M. A., Funderburk, S. J. & Cederbaum, S. D. (1978) Oculocutaneous albinism and mental disorder. A report of two autistic boys. *Human Heredity*, **28**, 81–85.

Scarone, S., Cazzullo, C. L. & Gambini, O. (1987) Asymmetry of lateralised hemispheric functions in schizophrenia. *British Journal of Psychiatry*, **151**, 15–17.

Sherrington, R., Brynjolfsson, J., Petursson, H., *et al* (1988) Location of a susceptibility locus for schizophrenia on chromosome 5. *Nature*, **336**, 164–167.

Sulestrowska, H. (1967) The psychiatric aspect of generalized albinism. *Polish Medical Journal*, **6**, 1276–1284.

Torrey, E. F. (1980) *Schizophrenia and Civilization*. London: Jason Aronson.

Wing, J. K., Cooper, J. E. & Sartorius, N. (1974) *The Measurement and Classification of Psychiatric Symptoms*. London: Cambridge University Press.

Witcop, C. J., Quevedo, W. C. & Fitzpatrick, T. B. (1978) Albinism. In *The Metabolic Basis of Inherited Disease* (eds J. B. Stanbury, J. B. Wyngaarden & D. S. Fredrickson). New York: McGraw-Hill.

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Erotomania in a Saudi Woman

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A case of de Clérambault syndrome, secondary to paranoid schizophrenia, in a Saudi woman is documented. Cultural factors were found ineffective in modifying or preventing symptoms. Erotomania appeared to arise from the same dynamics as those of the Western patients and to follow the same pattern.

G. G. de Clérambault (1942) described a syndrome he termed 'psychose passionelle'. This syndrome, which we term 'erotomania', is well reviewed by Enoch & Trethowan (1979). The syndrome usually affects women and consists of a patient's delusion that a public figure or brief acquaintance, usually older and of higher social rank, is in love with the patient. The target of the patient's delusion is frequently unaware of her/his beliefs and has done nothing to encourage them. Furthermore, the patient is fully convinced of being in amorous communication with the victim, who has been the first to fall in love and the first to make advances.

Two forms of de Clérambault syndrome have been differentiated: a pure or primary form, in which the onset is sudden and the disorder is limited entirely to erotomania: and a secondary form, in which the onset is gradual and the process superimposed on a pre-existing psychosis of a paranoid type. However, Ellis & Mellsop (1985) questioned the justification for the retention of the syndrome as a nosological entity in its primary form because of its rarity. Nevertheless, secondary erotomania is much commoner and has been associated with schizophrenia (Evans *et al*, 1982: Hayes & O'Shea, 1985), major depression (Raskin & Sullivan, 1974), bipolar affective disorder (Remington & Book, 1984), mental retardation (Greyson & Akhtar, 1977), and senile dementia (Drevets & Rubin, 1987).

Despite the numerous reports of the syndrome, there has been, to the author's knowledge, no case reported from the Middle East. The following case report documents some cultural factors and describes the syndrome in a Saudi female patient who was treated in Saudi Arabia.

Case report

A 28-year-old Saudi female patient first presented three years ago to the psychiatric out-patient clinic at Riyadh Armed Forces Hospital (RAFH). Following the initial assessment she was admitted to the psychiatric unit on in-patient basis. She was later admitted to RAFH on three other occasions during the past three years.

Her illness had started 14 years previously, and she had received various antipsychotics and electroconvulsive therapy (ECT) at different psychiatric hospitals in Saudi Arabia, Egypt, Iraq, and the UK, but had shown no response to treatment.

She is single and comes from the Eastern Province. She was a primary school teacher, but became unemployed after four years because of her illness. The father is a retired civilian who had a history of epilepsy, and the mother is an anxious woman. The patient has two younger sisters, who are well, and two cousins who suffer from mental illness.

During her admissions at RAFH the patient presented with symptoms of paranoid schizophrenia, mainly paranoid delusions, passivity feelings, thought insertion and broadcasting, but with no hallucinations. Her illness first started when the patient was at her intermediate school. She became convinced that her schoolmates were watching her because they were jealous of her beauty. They even used to watch her when going to the toilet to look at her sexual organs. She then started covering her eyes from people at home, even parents, sisters, and relatives. She explained this behaviour by saying that she was hiding the sins that she committed. She accused everybody of talking about her, claimed that her thoughts were not her own, and that anyone could read her thoughts by looking into her eyes. She accused her sister of hating her, because the patient was more beautiful than she, and believed that her sister wanted to kill her. Furthermore, she accused her father and grandfather, who lives with her at home, of spying on her in order to see her sexual organs, control her body, and make her masturbate. It must be noted that the patient was short, had a disproportionately large face, very much resembled her father, and was generally unattractive.

In regard to the symptom of erotomania, the delusion started suddenly on the ward at RAFH and was directed towards a Saudi junior psychiatrist. He was briefly involved in her treatment before he left the hospital and moved to another country. The patient falsely claimed that the doctor was the first to fall in love and was the first to make advances. She denied that he was married, which he was, and she believed that he had divorced his wife and had married her. The patient became very pre-occupied with his love and used to write him letters and poems, both in Arabic and English, that reflected her delusions and sexual fantasies. The theme of her emotions were nicely expressed in her numerous writings to her lover, and the following poem (translated from Arabic) is chosen as an example:

"It has been a long time since I last had a lover
My heart weeps for its deepest wounds
Oh my heart! life smiles upon everyone
But I search for a doctor to treat my bleeding heart . . .
Life may make us sad
Yet God will not abandon the ambitious: . . .
Even the doctor is cruel to the patient's heart
He wants me when it suits him, then walks away:
I sacrificed my life for my darling
Yet his wish is for my torment and in my tears is his delight
There is no existence of father, mother or even babe in arms . . ."

According to the patient she had another lover who was a pharmacist in another hospital but whom she has now left.

During her stay at RAFH the patient was treated with different antipsychotics but with no response. She received the maximum tolerable dose of both oral and depot formulations of the drugs. Physical investigations were normal except for the EEG, which suggested temporal lobe epilepsy. It showed a generalised spike wave bilaterally on hyperventilation, and the resting record showed bitemporal and frontotemporal low spikes and waves. Carbamazepine had no effect. Psychological testing showed a preserved personality, no evidence of deterioration of cognitive functioning, and a full-scale IQ of 133.

At present the patient receives no medication, lives with her family, still expresses her pathological symptoms but with no danger to herself or others. She is regularly reviewed at the out-patient clinic, and is admitted only for short periods should her family require a break.

Discussion

This case is typical of a patient suffering from paranoid schizophrenia with secondary erotomania. The course of the illness is chronic with little change in symptoms, and there has been no response to treatment. The delusion of love appears to have had a sudden onset; the victims of the patient's delusion, a psychiatrist and a pharmacist, were both working in hospitals and both had a brief acquaintance with the patient. This may suggest that the hospital environment, which is relatively free compared with life in the community in Saudi Arabia, was a factor in the development of the symptom. Although psychiatrists have been reported as the victims of patients with erotomania (Raskin & Sullivan, 1974), the change from one victim to another is remarkable in the case presented in that it is contrary to the reports of Enoch & Trethowan (1979) that the victim of the delusion remains constant.

Hollender & Callahan (1975) suggested that "erotomania lies beyond heterosexual love that begins with a school girl's fantasies, progresses to infatuation and then ultimately to mutual and abiding affection". Our patient appears to follow the same sequence of events and her delusional thinking seems to be largely shaped by feelings of being unloved by her schoolmates and later her family. These feelings were expressed in her writings, which stressed the hate of the family. Thus at times she adopted a religious attitude by imploring God to help her, or resorted to narcissistic love by believing in her false beauty and attributing the family's hate to jealousy. It must be emphasised that religious factors play an important role in the presentation of psychiatric illness in Saudi Arabia and tend to modify the clinical picture. In our case however religion had little effect on the clinical picture. In fact it did not prevent the manifestation of the pathology of the syndrome, particularly the sexual content, where the patient admitted to masturbation and to sexual love.

Although in a previous report (El-Assra, 1987) the author suggested that the Saudi family may play an important role in the maintenance and severity of a patient's illness, the family in our case of erotomania was responsible for neither the maintenance nor the severity of the syndrome. However, they may have played an early dynamic role in the development of the condition. A psychodynamic explanation suggested by Enoch & Trethowan (1979) for some of the Western patients suffering from the condition is probably appropriate in this case. Thus, the patient's conflict may be viewed as a struggle between her own natural drives and the notion that sex is taboo, dirty, and contrary to her father's wishes. The lover therefore represents an ideal father figure on whom she is able to project all the unconscious emotional and sexual drives.

References

de Clérambault, G. G. (1942) Les psychoses passionelles. In *Oevre Psychiatrique*. Paris: Presses Universitaires de France.

Drevets, W. C. & Rubin, E. H. (1987) Erotomania and senile dementia of Alzheimer type. *British Journal of Psychiatry*, **151**, 400–402.

El-Assra, A. (1987) A case of Gilles de la Tourette's syndrome in Saudi Arabia. *British Journal of Psychiatry*, **151**, 397–398.

Ellis, P. & Mellsop, G. (1985) De Clérambault's syndrome – a nosological entity? *British Journal of Psychiatry*, **146**, 90–93.

Enoch, M. D. & Trethowan, W. H. (1979) De Clérambault's syndrome. In *Uncommon Psychiatric Syndromes* (2nd edn) (eds M. D. Enoch & W. H. Trethowan). Bristol: John Wright.

Evans, D. L., Jeckel, L. L. & Sloh, N. H. (1982) Erotomania: a variant of pathological mourning. *Bulletin of the Menninger Clinic*, **46**, 507–520.

Greyson, B. & Akhtar, S. (1977) Erotomanic delusions in a mentally retarded patient. *American Journal of Psychiatry*, **134**, 325–326.

Hayes, M. & O'Shea, B. (1985) Erotomania in Schneider-positive schizophrenia – a case report. *British Journal of Psychiatry*, **146**, 661–663.

Hollender, M. H. & Callahan, A. S. (1975) Erotomania or de Clérambault syndrome. *Archives of General Psychiatry*, **32**, 1574–1576.

Raskin, D. E. & Sullivan, K. E. (1974) Erotomania. *American Journal of Psychiatry*, **131**, 1033–1035.

Remington, G. & Book, H. (1984) Case report of de Clérambault's syndrome, bipolar affective disorder and response to lithium. *American Journal of Psychiatry*, **141**, 1285–1287.

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Successful Treatment of Chronic Delusional Parasitosis

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A case of delusional parasitosis is presented in which a patient with classic symptoms of six years' duration responded to pimozide. Similarly chronic cases may be responsive to pimozide.

Delusional parasitosis (or 'delusional infestation') is a condition in which a person has the unshakeable belief of being infested with parasites (Reilly, 1988). The illness occurs most frequently in older women (Reilly & Batchelor, 1986), but may also affect younger men (Munro, 1988). Sufferers are able to describe in detail the activities of the parasite (e.g. burrowing or biting) and may produce 'evidence' such as fragments of skin. On occasions health authorities have been called upon to disinfest houses (Edwards, 1977; Lyell, 1983).

The patient should be carefully examined and preferably a dermatologist's opinion should be sought (Munro, 1978) to exclude actual infestation before the diagnosis is made. Psychiatric referral is usually strongly objected to by the patient (Tullet, 1965; Edwards, 1977; Reilly *et al*, 1978; Lyell, 1983), and suggestions have been made that the condition may be successfully treated by dermatologists without recourse to psychiatrists (Reilly *et al*, 1978; Lyell, 1983). Occasionally the delusion may be shared by more than one person (Edwards, 1977; Munro, 1988), and even group 'outbreaks' of imagined parasites may occur (Lyell, 1983). Delusional parasitosis may occur in any type of personality (Lyell, 1983), but frequently obsessional personalities are observed (Reilly & Batchelor, 1986). In addition, it may follow a genuine skin complaint (Tullet, 1965).

Case report

The patient, a 64-year-old married woman, presented at the psychiatric out-patient clinic with a six-year history of scratching and cutting her hair, being convinced that she was infested by "bugs". Her hair was extremely short, and she wore a wig when going out. She was not depressed or anxious, her appetite was good, but her sleep poor, with initial insomnia. Cognitive function was intact. Her belief of infestation began after cleaning a filthy house. Her general practitioner prescribed hydrocortisone butyrate scalp application and malathion shampoo, although there was no evidence of infestation. She was not referred to a dermatologist. Oxazepam was given without effect, then clomipramine (for obsessive symptoms). However, after an initial response (followed by poor compliance and relapse), clomipramine produced no further improvement. Behaviour therapy also failed to help.

The patient was from a large Roman Catholic family and previously worked as a domestic. She married when aged 48 years, after a brief courtship, to a 65-year-old man, whom she described as fatherly and strict. There was some marital disharmony, with verbal and physical abuse. The couple had no children. In fact the patient had expressed fears to her general practitioner concerning sex and pregnancy. She described herself as a shy person, and there is no evidence of previous obsessional personality. Past psychiatric history included treatment with amitryptyline for an episode of anxiety when she was 46 years old. Otherwise, her past medical history was unremarkable, as was her family history, except that one sister was admitted to hospital for a "nervous disorder" and had received treatment with diazepam.

At the psychiatric out-patient clinic, delusional parasitosis was diagnosed and treatment with pimozide commenced, initially at a dosage of 4 mg a day for one week. The dose was then doubled, but, unfortunately, this was poorly tolerated owing to dystonic side-effects, and so treatment was continued at the reduced dose of 4 mg a day. She was also referred for behaviour therapy. The patient improved: her hair began to grow and there was no evidence of delusions. After an eight-month follow-up period, she was discharged from the clinic and has since remained well on pimozide.

Discussion

The prognosis of delusional parasitosis was previously accepted as generally poor (Edwards, 1977; Reilly *et al*, 1978). However, pimozide is now a recognised treatment (Munro, 1978; Reilly *et al*, 1978; Lyell, 1983). Pimozide is a neuroleptic drug of the diphenylbutylpiperidine group administered orally in a once-daily dose. It can cause extrapyramidal side-effects, but these are generally considerably less severe than with other neuroleptics.

A recent follow-up study (Lindskov & Baadsgaard, 1985) demonstrated remission of symptoms with pimozide, and in some patients this lasted for significant periods even after discontinuation of the drug. However, delusional parasitosis may recur if pimozide is stopped (Munro, 1978). This case demonstrates pimozide as an effective treatment even when the delusional parasitosis is long-standing.

References

EDWARDS, R. (1977) Editorial. *British Medical Journal*, *i*, 790–791.

LINDSKOV, R. & BAADSGAARD, O. (1985) Delusions of infestation treated with pimozide: a follow-up study. *Acta Dermato-Venereologica (Stockholm)*, **65**, 267–270.

LYELL, A. (1983) Delusions of parasitosis. *British Journal of Dermatology*, **108**, 485–499.

MUNRO, A. (1978) Monosymptomatic hypochondriacal psychosis manifesting as delusional parasitosis. *Archives of Dermatology*, 114, 940–943.

—— (1988) Monosymptomatic hypochondriacal psychosis. *British Journal of Psychiatry*, **153** (suppl. 2), 37–40.

REILLY, T. M. (1988) Delusional infestation. *British Journal of Psychiatry*, **153** (suppl. 2), 44–46.

——, JOPLING, W. H. & BEARD, A. V. (1978) Successful treatment with pimozide of delusional parasitosis. *British Journal of Dermatology*, **98**, 457–459.

——, BATCHELOR, D. H. (1986) The presentation and treatment of delusional parasitosis: a dermatological perspective. *International Clinical Psychopharmacology*, 1, 340–353.

TULLET, G. L. (1965) Delusions of parasitosis. *British Journal of Dermatology*, **77**, 448–455.

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Subacute Sclerosing Panencephalitis Presenting as Schizophreniform Psychosis

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A case of a 21-year-old woman with subacute sclerosing panencephalitis presenting with paranoid schizophreniform symptoms is presented. The relationship between viral encephalitis and psychiatric symptoms is briefly considered.

Most psychotic illnesses associated with underlying brain disease present with clouding of consciousness or neurological signs to suggest their organic basis. It has long been known, however, that encephalitis may present with a psychosis in the absence of any delirium. Torrey (1986) summarised reports of 22 such cases. He found that a number of neuropathic viruses had been implicated, including herpes simplex, Epstein–Barr, cytomegalovirus, measles, and rubella. To this list can be added human immunodeficiency virus (HIV) (*Biological Psychiatry*, 1986). Torrey found that nearly all cases went on to develop neurological features to suggest their encephalitic origin.

Subacute sclerosing panencephalitis (SSPE) is a slow viral infection of the central nervous system, with degeneration of grey matter, and loss of white matter. It was initially thought due to herpes simplex and it was not until 1967 that Connolly *et al* and Legg established the link with the measles virus. The exact pathogenesis remains unclear, but it is felt by Hall and Chopin (1979) that an inability of infected brain cells to produce the specific matrix (m) protein necessary for viral budding leads to persistence in the cell and spread by direct cell-to-cell contact. The virus is thus not effectively presented to the immune system, preventing clearance.

The clinical features of the disease have been divided into four stages by Jabbour *et al* (1969): stage I, with behavioural and cognitive changes such as forgetfulness and irritability; stage II, with convulsive motor signs such as myoclonus of the head, limbs and trunk; stage III, with coma, opisthotonos, decerebrate rigidity, and irregular respiration; and stage IV, with loss of cortical function, wandering eyes, and frequent myoclonus. Psychotic symptoms have been less well documented in the literature.

Salib (1988) documented a 21-year-old man who presented with a schizophrenic-like state characterised by dysmorphophobic features. We report a case in which paranoid schizophreniform symptoms were the initial presenting features of SSPE.

Case report

A 21-year-old single mother had initially been referred to a community psychiatric clinic. According to the patient and her mother, problems started two months earlier when her common-law husband had left, after five years. Since then, she had been gradually less able to care for her 18-month-old daughter, and had felt people were "after her", causing her to be fearful and attempt to hide in company. She also believed people could read her mind and that "someone" was tampering with her thoughts.

There was no past psychiatric history or use of prescription or illegal drugs. There was no family psychiatric history. Her developmental history had been unremarkable, and she had been described as popular and socially active. She had had only one heterosexual relationship.

At initial presentation she was fearful and perplexed, with occasional echolalia. Delusions of self-reference and persecution were present. The patient thought that radio announcers were talking about her and communicating with the police, who were following and observing her with hidden cameras. Thought insertion and broadcast were also present, the patient believing the police were able to read her thoughts and were putting the idea of committing a crime into her mind. There were no perceptual abnormalities. Cognitive testing revealed normal orientation, memory function, and visuospatial skills. A diagnosis of schizophreniform disorder was made, and fluphenazine HCL (10 mg b.d.) commenced.

She was seen regularly at the community clinic after her initial contact and her psychotic symptoms improved, but she developed troublesome rigidity and bradykinesia. This persisted despite regular benztropine (4 mg/day) and reduction of fluphenazine to 2.5 mg/day. Seven weeks after her initial assessment she started to become withdrawn and agitated, with a re-emergence of echolalia. Four days later she was noted to be disorientated and had urinary hesitancy, and she was transferred to a general hospital psychiatric unit. It was thought she had relapsed in her psychotic illness, with the possible complication of anticholinergic toxicity.

On admission to a general hospital psychiatric unit her mental status examination was consistent with a severe delirium with the presence of partial receptive dysphasia, disorientation, dyscalculia, and short-term memory deficits. Marked echolalia and perseveration were present.

The patient walked on the balls of her feet with a shuffling motion, and had bilateral grasp reflexes and increased tone in both arms.

The aetiology of the delirium was unclear and all drugs were ceased while a diagnostic evaluation was commenced. Initial haematological, biochemical, and thyroid studies were normal. An EEG done 24 hours after admission showed prominent frontotemporal theta and delta activity consistent with an organic brain syndrome. A computerised tomography head scan performed two days after admission demonstrated cerebral atrophy with widened sulci and a slightly dilated ventricular system.

In view of these abnormal findings and her lack of symptomatic improvement she was investigated for specific possible infective and metabolic causes of rapid cerebral degeneration. Examination of cerebrospinal fluid (CSF) showed elevated protein (0.57/gm/1, normal range 0.16–0.5/gm/1), elevated immunoglobulin levels, and the presence of oligoclonal bands. Both CSF (titre 1/32) and serum (titre 1/320) measles complement fixation titres were raised. There was no CSF or serological evidence of syphilis or rubella. HIV antibody was not detected. Investigations for various leucodystrophies were negative.

A repeat EEG performed seven days after admission showed some evidence of brief bursts of high-amplitude slow waves followed by periods of a relatively flat trace seen frequently in SSPE (Zilber *et al*, 1983). At this time she was also noted to have developed myoclonic jerking in her left leg and arm.

Further history from the family revealed a childhood episode of measles when she was one.

The diagnosis of SSPE was made on the basis of: (a) the progressive neurological deterioration with myoclonic jerks; (b) a CSF measles titre of >1:4 and serum measles titre of >1:256; (c) oligoclonal bands and elevated protein in the CSF; and (d) the EEG findings.

The patient's general condition continued to deteriorate, and two weeks after admission she was bedridden, doubly incontinent, and responding only to painful stimuli. She developed decorticate posturing with generalised hypertonicity, hyper-reflexia, and bilateral extensor plantar responses.

She was commenced on a trial of the antiviral drugs inosiplex and interferon, as previously reported by Harbord *et al* (1988), with little change in her condition. These medications were ceased after three months, and she died of pneumonia one month later.

Central nervous system autopsy findings were of generalised grey matter atrophy, diffuse demyelination, and inclusion bodies in both glial cells and nuerons. These findings are all consistent with SSPE (Taylor *et al*, 1984).

Discussion

The present case serves as a reminder of the capability of a viral encephalitis to present as a psychosis without features of delirium. The patient's initial psychotic symptoms and clear sensorium, together with a deterioration in personal functioning following a major psychosocial stressor, was suggestive of a schizophreniform disorder. However, the termination of the relationship with her boyfriend may have been a consequence of her illness rather than being causal.

Similarly, her symptomatic improvement with fluphenazine was consistent with a typical schizophrenic illness, and her extrapyramidal symptoms were initially regarded as a side-effect. In retrospect these could have been an early motor manifestation of her disease. It was not until she developed definite cognitive impairment with neurological signs that an underlying organic cause became obvious.

How frequently viral encephalitis presents as a psychiatric illness is not clear, but Stewart & Baldessarini (1976) identified four such cases presenting over two years to a large general hospital. Torrey (1986) suggests that the following should alert the doctor to a possible encephalitic origin:

(a) presentation or development of signs of influenza, fever or headache, immediately preceding or concurrent with psychotic symptoms, (b) extremely disinhibited behaviour, (c) rapid onset of psychosis, (d) seizure-like activity, vague neurological symptoms, or neurological signs such as ataxia, nystagmus or pupillary changes.

SSPE is itself a rare disorder, with an annual incidence of 0.2 per million of the total population in the United Kingdom (Kipps, 1983). The disease was initially thought to affect only children and adolescents; however, the development of reliable diagnostic criteria enabled the first definite adult onset case to be reported by Cape *et al* (1973).

The prognosis for SSPE is poor, with a 55% mortality in the first two years after diagnosis and only 10–28% surviving over four years (Haddad *et al*, 1977), generally with severe handicaps. Spontaneous remissions have been reported in 5% of cases (Risk & Haddad, 1979).

SSPE should form part of the differential diagnosis in psychotic illnesses where an underlying encephalitis is suspected in both adolescents and young adults.

References

BIOLOGICAL PSYCHIATRY (1986) Neuropsychiatry of acquired immunodeficiency syndrome. *Biological Psychiatry*, **21**, 1357–1359.

CAPE, C. A., MARTINEZ, A. J., ROBERTSON, J. T., *et al* (1973) Adult onset of subacute sclerosing panencephalitis. *Archives of Neurology*, **28**, 124–127.

CONNOLLY, J. H., ALLEN, I. V. & HURWITZ, L. J. (1967) Measles-virus antibody and antigen in subacute sclerosing panencephalitis. *Lancet*, *i*, 542–544.

HADDAD, F. S., RISK, W. S. & JABBOUR, J. T. (1977) Subacute sclerosing panencephalitis in the Middle East: report of 99 cases. *Annals of Neurology*, **1**, 211–217.

HALL, W. W. & CHOPIN, P. W. (1979) Evidence for lack of synthesis for the M polypeptide of measles virus in brain cells in subacute sclerosing panencephalitis. *Virology*, **99**, 443–447.

HARBORD, M. G., JONES, T., HICKS, E. P., *et al* (1988) Intra-ventricular administration of interferon and administration of methisoprinal by mouth in the treatment of adult-onset subacute sclerosing panencephalitis. *Medical Journal of Australia*, **148**, 467–473.

JABBOUR, J. T., GARCIA, J. H., LEMMI, H., *et al* (1969) Subacute sclerosing panencephalitis, a multidisciplinary study of 8 cases. *Journal of the American Medical Association*, **297**, 2248–2254.

KIPPS, A., DICK, G. & MOOCHE, J. W. (1983) Measles and the central nervous system. *Lancet*, *ii*, 1406–1410.

LEGG, N. J. (1967) Virus antibodies in subacute sclerosing panencephalitis: a study of 22 patients. *British Medical Journal*, *iii*, 350–352.

RISK, W. S. HADDAD, F. S. (1979) The variable natural history of subacute sclerosing panencephalitis. A study of 188 cases from the Middle East. *Archives of Neurology*, **36**, 610–614.

SALIB, E. A. (1988) Subacute sclerosing panencephalitis (S.S.P.E.) presenting at the age of 21 as a schizophrenia-like state with bizarre dysmorphophobic features. *British Journal of Psychiatry*, **152**, 709–710.

STEWART, R. M. & BALDESSARINI, R. J. (1976) Viral encephalopathy and psychosis. *American Journal of Psychiatry*, **133**, 717.

TAYLOR, W. J., DURANT, R. H. & DYKEN, P. R. (1984) Treatment of subacute sclerosing panencephalitis: an overview. *Drug Intelligence and Clinical Pharmacy*, **18**, 375–380.

TORREY, E. F. (1986) Functional psychosis and viral encephalitis. *Integrated Psychiatry*, **4**, 224–236.

ZILBER, N., RANNON, L., ALTER, M., *et al* (1983) Measles, measles vaccination and risk of subacute sclerosing panencephalitis (S.S.P.E.). *Neurology (Cleveland)*, **33**, 1558–1564.

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Neurosyphilis Presenting as Psychiatric Disorders

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The authors present two patients with neurosyphilis who presented with psychiatric disorders and who both benefited from penicillin therapy. Increases in such cases may be expected.

Neurosyphilis, 'the great imitator', may resemble any medical or psychiatric disorder. It remains an important and frequently encountered entity. Two cases presenting unusual features are described.

Case reports

Case 1

A 68-year-old Jewish male of Sephardic origin was admitted because of a depressive episode associated with suicidal ideation. There was no family history of mental disorder. He worked as a car mechanic and as a taxi-driver. His familial, social, and occupational record showed no disturbances of functioning. He had suffered from diabetes mellitus for 20 years and was treated by glibenclamide (5 mg daily) and metformin HCl (850 mg twice daily).

Over the previous 11 years he had had several depressive episodes and one manic episode, and had several times been admitted to psychiatric hospitals. Two months before his present admission he was discharged from another psychiatric hospital where he was treated with various antidepressants, but with only moderate amelioration of symptoms. One month later he complained of insomnia, decreased appetite, guilt feelings, and despair. He lost his desire to live, and was pre-occupied with suicidal ideation. At this stage he was admitted to our ward. On admission his consciousness was clear and he was co-operative. His speech and movements were slow. The affect was depressed and congruent with his thoughts. His thinking was slow, organised, and the content was despair at the loss of his ability and strength to cope with his disease. He expressed guilt feelings concerning his dependency on his family. His perception was intact and his intelligence was average. His long-term memory was affected. His concentration was poor. He was disorientated in time and partially in place. He retained judgement and insight. On physical examination the pupils were round and symmetrical. Light and accommodation reflexes were normal. Areflexia of the lower limbs was found. Chest X-ray was normal. The symptoms described above raised the question of an organic brain syndrome associated with the depression, and we performed some laboratory and auxilliary examinations.

Computerised tomography of the brain revealed cortical atrophy. Serological tests for syphilis were positive for both the haemagglutination test (TPHA) and the immunofluorescent antibody test (FTA–ABS). Cerebro-spinal fluid obtained on lumbar puncture revealed elevated protein and 14 leucocytes per millilitre. Based on these findings the diagnosis of neurosyphilis was made. The patient was treated with Benzathine penicillin (2 400 000 units i.m. once a week) for three weeks and amitryptyline (125 mg daily). His depression disappeared gradually, and he was discharged in full remission.

Follow-up lumbar puncture three months after discharge revealed a significant decrease in the number of white blood cells (3 leucocytes per millilitre) and protein levels. Mental status examination six months after discharge was normal except for slight impairment of long-term memory. He returned to his prior level of functioning.

When the patient was told about the clinical findings, he recalled that during World War II, while serving in the British Army in Egypt, he contacted syphilis for which he received bismuth therapy.

Case 2

A 39-year-old divorced woman was admitted because of acute psychosis with delusions, hallucinations, impaired judgement, and a gradual loss of ability to function a year previous to her admission. This was her first admission to a psychiatric hospital.

The patient was not fully orientated in place and time, and she had a shallow and inappropriate affect, loosening of associations, blocking, bizarre megalomanic delusions of a religious nature (bringing peace to Jerusalem by reconstructing the Temple in the Holy City of Jerusalem, and by being a kind of Messiah), auditory hallucinations, derealisation, disturbed concentration and judgement, and lack of insight.

Medical history revealed three spontaneous abortions. On physical examination the pupils were round and symmetrical; light and accommodation reflexes were normal. Fundoscopy was negative. On neurological examination no pathological findings were found. A systolic murmur (2/6) was found over the apex on auscultation. Chest X-ray was normal. Routine laboratory tests revealed hypochromic microcytic anaemia due to iron deficiency; venereal disease and TPHA tests were positive.

Haloperidol (40 mg daily) was initiated as antipsychotic treatment, with a gradual disappearance of the hallucinations and delusions, and improvement of concentration and judgement. The affect remained shallow and inappropriate. Concomitantly, suspecting neurosyphilis, a complete serological battery was performed including Nelson *Treponema pallidum* immobilisation test, FTA–ABS test, and Rappaport test. All were found to be positive. The slide flocculation test was positive up to a titre of 1:2.

Lumbar puncture revealed elevated levels of protein and chloride, and 10 leucocytes per millilitre. Computerised tomography of the brain revealed a small localised area of low density in the left posterior thalamus without surrounding oedema or pressure on neighbouring areas. The neurosurgical consultant did not consider this finding to be clinically significant.

Treatment with intramuscular injections of penicillin G (1 000 000 units daily) for 15 consecutive days was initiated. Twelve days after termination of treatment the Rappaport test became negative and the VDRL weakly positive. Follow-up lumbar puncture four months after discharge revealed a decrease in the number of white blood cells and protein. Her mental status examination at three, six, and nine months revealed mild lability of affect. She denied ever having had syphilis.

Discussion

Neurosyphilis, developing 5–15 years after initial infection (Kaplan *et al*, 1980; Rundell & Wise, 1985), may present as virtually any psychiatric disorder. Moreover, combined or atypical forms of neurosyphilis may display mixed findings. Incidental partial treatment with penicillin (given for other disorders) further complicates the clinical picture

(Joyce-Clarke & Molteno, 1978; *Morbidity, Mortality Weekly Report*, 1980).

Changes in personality, affect, sensorium, and intellect are cardinal findings on psychiatric examination (Isselbacher *et al*, 1980). Other features can be found on physical examination, for example cranial nerve dysfunction and pupillary changes.

This entity poses a complex diagnostic problem for the clinician because of the difficulty in obtaining a reliable history from the patient. The second patient denied having had syphilis, and the first patient was embarrassed about having the disease in the past. Both patients presented with functional disorders, one with schizophreniform episode and the other with bipolar affective disorder. In each case there were unusual features. In the first case there was an unusually long interval (approximately 30 years) between putative infection and clinical presentation. An 11-year history of bipolar disorder in the absence of any progressive deterioration is an atypical psychiatric manifestation. The second patient's neurological examination was normal, although neurological abnormalities have been reported in over 90% of patients with neurosyphilis.

The variability of presentation places an increasingly greater emphasis on reliable diagnostic criteria. Hooshmand *et al* (1972) have suggested that in the absence of neurological features, FTA-ABS tests should be positive in cerebrospinal fluid (CSF) as well as in blood, and that CSF should contain over 5 leucocytes per millilitre in the absence of bacterial or viral meningitis. This was so in both of our cases. The computerised tomography findings of the two patients did not provide specific diagnostic data for neurosyphilis, and this is in accordance with Godt *et al*'s (1979) findings.

Because neurosyphilis may mimic any psychiatric disorder the psychiatrist must be suspicious; the diagnosis can be confirmed only by taking into account the clinical findings and course, the serological tests, and the results of therapy.

Treatment of neurosyphilis is vital, as most of its manifestations are potentially reversible. Penicillin remains the drug of choice, although different treatment regimes have been recommended (Godt *et al* 1979; Simon, 1985; Rundell & Wise, 1985). Simon (1985) suggested that documentation of CSF resolution over the months following penicillin therapy is required to confirm the effectiveness of the treatment.

References

Godt, P., Stoeppler, L., Wischer, U., *et al* (1979) The value of computed tomography in cerebral syphilis. *Neuroradiology*, **18**, 197–200.

Hooshmand, H., Escobar, M. R. & Kopf, S. W. (1972) Neurosyphilis, a study of 241 patients. *Journal of American Medical Association*; **219**, 726–729.

Isselbacher, K. H., Adams, R. D., Braunwald, E., *et al* (1980) *Harrison's Principles of Internal Medicine*, p. 720. New York: McGraw-Hill.

Joyce-Clarke, N. & Molteno, A. B. (1978) Modified neurosyphilis in the Cape Peninsula. *South Africa Medical Journal*, **53**, 10–14.

Kaplan, H. I., Freedman, A. M. & Sadock, B. J. (1980) *Comprehensive Textbook of Psychiatry* (3rd edn), vol. 2, p. 1457. Baltimore: Williams and Wilkins.

Morbidity, Mortality Weekly Report (1980) Syphilis trends in the United States. *Morbidity, Mortality Weekly Report*, **30**, 441–449.

Rundell, J. R. & Wise, M. G. (1985) Neurosyphilis: a psychiatric perspective. *Psychosomatics*, **26**, 287–295.

Simon, R. P. (1985) Neurosyphilis. *Archives of Neurology*, **42**, 606–613.

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Neuroleptic Malignant Syndrome with Trifluperidol

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In a case of NMS subsequent to administration of trifluperidol to a young man, the patient responded remarkably quickly to bromocriptine. The authors point out the deficiencies in the diagnostic criteria, which need further refinement for a better understanding of the syndrome.

Neuroleptic malignant syndrome (NMS) is a rare and potentially fatal idiosyncratic reaction to neuroleptic drugs. The syndrome is characterised by severe muscular rigidity, fever, autonomic dysfunction, and alteration of mental state (Levenson, 1985). The understanding of the pathogenesis of NMS remains speculative. The syndrome can rapidly develop into a life-threatening condition, which is fatal in up to 22% of cases (Shalev & Munitz, 1986), and hence there is a great need for an early recognition and prompt, adequate treatment. Following resolution of the syndrome, neuroleptics can be successfully reintroduced in most cases (Mueller *et al* 1983; Levenson, 1985). We report the following because a search of the literature did not reveal any case of NMS following administration of trifluperidol, and the response to bromocriptine was remarkably rapid.

Case report

A 26-year-old man was referred with a six-week history of irrelevant speech, socially disruptive behaviour, and neglect of personal care, of an acute onset; within three days of the onset he had been admitted to a state mental hospital, where oral antipsychotics had been started. The patient developed low-grade fever with wide fluctuation in blood pressure, but there was no change in the psychotic features. After referral he was put on i.m. trifluperidol (5 mg, 8 hourly). Within 24 hours the patient became rigid, mute, unresponsive, and developed difficulty in swallowing.

The patient had attempted suicide two years previously; his mother suffered from a bipolar affective disorder, and one sister and one brother from schizophrenic illness.

The patient was referred to our hospital as a case of acute psychotic episode with a probable phaeochromocytoma. On admission he was found to be completely unresponsive, with severe rigidity of all voluntary muscles. He had marked autonomic hyperactivity, with profuse diaphoresis, fluctuating blood pressure, dilated pupils, and moderate fever.

During the first few days in hospital his vital signs showed marked fluctuation: pulse rate 74–160 beats/minute, blood pressure 110/70–170/110 mmHg, respiratory rate 14–36/minute, and temperature 36–38.6°C. Investigations revealed a white blood cell count of 24 000/mm^3, with a marked shift to the left. The other tests for pyrexia, and liver and renal functions were normal. Chest X-ray, ECG and vanillylmandelic acid studies for phaeochromocytoma were normal. Levels of creatinine phosphokinase (CPK) were not determined, yet bromocriptine was started orally (2 mg t.d.s.). Within 72 hours the patient's rigidity began to diminish, his vital signs stabilised, he became afebrile, and he started communicating. His raised leucocyte count fell concomitantly with his clinical recovery and, by the tenth day, the patient was nearly normal, except for mild cognitive deficits in immediate memory and attention span. A psychometric evaluation of cognitive functions revealed mild impairment. Throughout his stay in our hospital, antispychotics had not been administered to the patient. The final diagnosis was acute schizophrenic episode with neuroleptic malignant syndrome. The patient was kept in the hospital for one month, and at the time of discharge was completely asymptomatic. On subsequent follow-up his blood pressure and mental state were found to be normal.

Discussion

The previous case reports of NMS have shown a wide variability in the clinical picture and many authors have reported 'atypical' or 'incomplete' forms of NMS (Goulun *et al*, 1983; Misiazek & Potter, 1985). Caroff (1980) considered rigidity, hyperpyrexia, autonomic dysfunction, and alteration of consciousness of varying degrees as the *sine qua non* of NMS. Levenson (1985) has proposed criteria for the diagnosis of NMS. Major manifestations include fever, rigidity, and raised levels of CPK, while minor manifestations include tachycardia, abnormal blood pressure, tachypnoea, altered consciousness, diaphoresis, and leucocytosis. The presence of all the three major, or two major and four minor, criteria is essential to substantiate a diagnosis of NMS (Levenson, 1985). In our patient, two major criteria, fever and rigidity, and all the minor criteria were present. CPK levels were not studied, but then CPK may only be mildly elevated in NMS, as reported by McCarthy *et al* (1988). Even in Levenson's study, 8 out of the 53 reported cases had shown only mild elevation in CPK levels. An elevated CPK level may be a sensitive sign of NMS, but it lacks specificity. According to Pasternak *et al* (1987), a two- to three-fold elevation of total CPK may follow an intramuscular injection, other causes of CPK elevation being acute myocardial infarction, muscular dystrophies, surgery, cardiac catheterisation, hypothyroidism, electrical cardioversion, stroke, and skeletal muscle damage secondary to trauma, convulsion and prolonged immobilisation.

In our patient, the fever could not be explained in terms of any other illness as blood culture and other investigations for pyrexia were normal. Signs of autonomic dysfunction had appeared first, followed by fever and rigidity, and this has been suggested as the temporal sequence in NMS (Guze & Baxter, 1985). Others have, however, considered it incorrect to rely on the presence of any typical sequence of symptoms leading up to full-blown NMS (Shalev & Munitz, 1986).

The incidence of organic brain disease has been reported to be high in patients who develop NMS (Caroff, 1980; Shalev & Munitz, 1986). Although our patient did not have any organic brain disorder as such, psychometry did reveal mild cognitive deficits during the recovery phase, which can be understood as a consequence of the disease itself.

It appears that NMS has been often unrecognised and underdiagnosed (Caroff, 1980), owing to ignorance regarding the syndrome, lack of clear-cut diagnostic criteria, and wide variability in the clinical presentation. Even Levenson's diagnostic criteria are not free from criticism. They do not seem to be mutually exclusive; for instance, any non-specific fever (a major manifestation) can cause tachycardia, tachypnoea, and diaphoresis (minor manifestations). There is no clear cut-off point for elevated levels of CPK, thus reducing its specificity. Refinements in the diagnostic criteria may be helpful in recognising and understanding this potentially fatal complication of neuroleptic use.

References

Caroff, N. (1980) The neuroleptic malignant syndrome. *Journal of Clinical Psychology*, **41**, 79–83.

Goulun, M., de Rohan Chabot, P., Elkhaart, D., *et al* (1983) Beneficial effects of dantrolene in the treatment of neurolepetic malignant syndrome: a report of two cases. *Neurology*, **33**, 516–518.

Guze, G. H. & Baxter, L. R. J. (1985). Neuroleptic malignant syndrome. *New England Journal of Medicine*, **313**, 163–166.

Levenson, J. L. (1985) Neuroleptic malignant syndrome. *American Journal of Psychiatry*, **142**, 1137–1145.

McCarthy, A., Bourke, S., Fahy, J., *et al* (1988) Fatal recurrence of neuroleptic malignant syndrome. *British Journal of Psychiatry*, **152**, 558–559.

Misiazek, J. J. & Potter, R. L. (1985) A typical neuroleptic malignant syndrome responsive to conservative treatment. *Psychosomatics*, **26**, 62–66.

Mueller, P. S., Vester, J. W. & Fermaglich, J. (1983) Neuroleptic malignant syndrome. Successful treatment with bromocriptine. *Journal of American Medical Association*, **249**, 396–398.

Pasternak, R. C., Braunwald, E. & Alpert, J. S. (1987) Acute myocardial infarction. In *Harrison's Principles of Internal Medicine* (eds E. Braunwald *et al*). New York: McGraw Hill.

Shalev, A. & Munitz, H. (1986) The neuroleptic malignant syndrome: agent and host interactions. *Acta Psychiatrica Scandinavica*, **73**, 337–347.

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Contents: Molecular genetics of alcoholism/Multiple personality disorder/How many sheltered housing places?/Affective 'switch mechanisms'/The opiate prescribing debate continued/Case conference correction/Distress caused by miscarriage/CPK levels and neuroleptic malignant syndrome/ Paradoxical intervention/Psychiatric despotism?/ Anorexia nervosa and Chinese food/Oculogyric crises and schizophrenia/Caution about sorcery/ Benign intercranial hypertension and repeated self-mutilation

Molecular genetics of alcoholism

SIR: In their impressive review Mullan & Murray (*Journal*, May 1989, **154**, 591–595) have confined themselves to the impact of molecular genetics on understanding and nosology of psychotic disorders. The same techniques, however, can be extended to other biologically determined disorders in psychiatry. We are constantly moving from diagnostic categories with only face and descriptive validity to aetiologically homogeneous nosologic entities, which are defined on the solid foundation of construct and predictive validity. The application of 'new genetics' is a powerful tool in teasing out aetiologically heterogeneous categories which were hitherto lumped together on the basis of superficial chemical resemblance.

In the field of alcoholism, the recent genetic epidemiological work done by Cloninger and his co-workers has supported genetic heterogeneity in alcoholism (Bohman *et al*, 1987; Cloninger, 1987; Gilligan *et al*, 1987). Despite the suggestion that at least some subtypes of alcoholism are genetically mediated, it is not yet certain as to what is inherited. The vulnerability to alcohol use may be transmitted independently of vulnerability to develop alcohol-related pathologies. The most simple model is reductionist but practical, i.e. that of inherited abnormal biochemistry predisposing to the development of physiological addiction. However, there is little evidence that the gross rate of alcohol metabolism is itself associated with the risk for developing alcoholism. Recent pharmacogenetic studies in animals have shown that the relationship between initial sensitivity to ethanol (as measured by ataxia, body temperature, and disruption of motor performance) and the ability of this drug to serve as a positive reinforcer is minimal, thus distinguishing the specific intoxicating effects of ethanol from its reinforcement effects (George & Goldberg, 1989).

It is highly likely that the genetic influence is one of specific predisposition to the development of alcoholism, in view of these findings. The recent genetic epidemiological work advocates the interesting possibility of an aetiologically homogeneous subgroup (Type II) in which most of the liability to alcoholism is transmitted by a single dominant gene (Gilligan *et al*, 1987; Craufurd, 1989). Furthermore, keeping in view that the Type II alcoholism is consistently associated with the male sex and the conspicuous absence of father to daughter transmission of this subtype, one could hypothesise that the dominant gene is probably located on the sex-determining region of the Y chromosome.

This hypothesis would be of great heuristic importance as a basis for future molecular genetic studies. Prior evidence for the hypothesis that the marker is on a particular chromosome can be of great help in localisation and subsequent mapping of a genetic locus (Baron & Rainer, 1988). Anonymous Y-linked DNA probes may be employed to exclude or affirm Y-linkage in those pedigrees that show no father–daughter transmission and where no females are affected. Testing of this hypothesis would be helpful in the development of reliable diagnostic criteria for the correct classification of the alcoholic subtypes, besides providing construct validators for Cloninger's typology.

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References

BARON, M. & RAINER, J. D. (1988) Molecular genetics and human disease: implications for modern psychiatric research and practice. *British Journal of Psychiatry*, **152**, 741–753.

BOHMAN, M., CLONINGER, C. R., SIGVARDSSON, S. *et al* (1987) The genetics of alcoholism and related disorders. *Journal of Psychiatric Research*, **21**, 447–452.

CLONINGER, C. R. (1987) Neurogenetic adaptive mechanisms in alcoholism. *Science*, **236**, 410–416.

CRAUFURD, D. (1989) Psychiatric genetics. *Current Opinion in Psychiatry*, **2**, 101–105.

GILLIGAN, S. B., REICH, T. & CLONINGER, C. R. (1987) Etiologic heterogeneity in alcoholism. *Genetic Epidemiology*, **4**, 395–414.

GEORGE, F. R. & GOLDBERG, S. R. (1989) Genetic approaches to the analysis of addiction processes. *Trends in Pharmacological Sciences*, **10**, 78–83.

Multiple personality disorder

SIR: Fahy (*Journal*, October 1988, **153**, 597–606) provided a useful critical review of the highly peculiar nosological category of multiple personality disorder (MPD). I suggest that, taking into account the many uniquely odd characteristics of this diagnosis, an alternative hypothesis is needed to account for this most rum condition.

More than any other diagnosis, patients allegedly suffering from it have become major media celebrities, fêted in the popular media. In the history of medicine or psychology, has any condition been so reliably rewarding to those supposedly 'suffering' from it; or to the physicians and psychologists who attend them?

The condition arouses excessive interest and excessive claims. Clinicians reporting such cases usually show an infatuation with them. Like new parents, they can never miss an opportunity to show photographs, movies, or videos of their uniquely talented offspring, or to tell you of their latest cute trick.

The distribution of MPD is bizarre. There is no normal distribution of cases. I've never met a clinician who, over any significant period of time, has seen just one case. The vast majority of talented, sensitive, observant clinicians have never seen a case at all. A very small number of clinicians report the great majority of case reports.

Spontaneous remission is probably the norm, unless the patient becomes engaged with a clinician already primed and interested in the condition. It seems to be one of the few conditions which almost invariably get worse in therapy; the extent of the patient's pathology is directly proportional to its amount and intensity, and shows the most evolved and disturbed anomalies in the most intensively studied cases. It appears to be the norm that further 'personalities', often more entertaining and rewarding for the audience, emerge in therapy.

My hypothesis is that MPD is an iatrogenic, largely culture-bound disorder, with some resemblances to folie à deux, arising when a bright, suggestible patient meets a bright, suggestible physician convinced that MPD is an important diagnosis. Selective reinforcement of symptoms, unconscious and conscious, progressively shapes the symptoms and behaviour of the patient, and the depiction of MPD is elaborated and reinforced. Patients usually show clear primary or secondary gain, but this is often not noted or acknowledged by their therapists, whose own secondary (and maybe primary?) gains are similarly covert.

Procedures regularly followed, such as naming the alternative 'personalities' and having long, carefully recorded conversations with them, serve to preserve and reify these otherwise transient situations, locking them into publicly shared 'reality'. Any 'as-if' quality to the original experiences is stamped out. The inevitable audio and videotaping provides a handy record of the nuances of the successful performance, and an aide-memoire for both participants, to enable the maintenance of a consistent portrayal.

There is no convincing evidence that MPD is a naturally occurring condition, let alone a distinct diagnosis. It is a symptom complex that may be superimposed on other psychopathologies, consequent upon the unfortunate matching of a susceptible patient with a susceptible therapist and trainer. The diagnosis is dysfunctional, focusing attention selectively in a way that will almost invariably worsen the condition, rather than improving it. It occurs in the context of the availability of lengthy psychotherapy. Where the health care system or health insurance does not sponsor this indulgence, the condition simply does not occur.

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How many sheltered housing places?

SIR: We recently conducted in Montréal a survey comparable to the Glasgow Rehabilitation Survey (Livingston & Bryson, *Journal*, May 1989, **154**, 620–624), and found a strikingly similar rate (29%) of patients who would be able to live in the community. However, our consultants estimated that more sheltered housing would be needed, especially group homes directly supervised by nursing staff.

Canada's health and social care systems grant universal access to services. In Montréal, all psychiatric in-patient facilities are public. The recently revised provincial mental health policies call for further transfer of mental hospital in-patients to the community. Hôpital Louis-H. Lafontaine is a 2000-bed mental hospital currently covering a catchment population of 330 000. However, until 5 years ago it also served as a long-term facility for the French-speaking population of Greater Montréal (2.8 million inhabitants). The hospital population has steadily declined since 1960, when the census indicated 5621 in-patients. Our survey was conducted on a random sample of 300 of the 831 in-patients aged 18–60 with a primary functional psychiatric diagnosis. A short questionnaire was sent to the consultants. We provided a choice of operationally-defined residential facilities, and asked the consultants to indicate the most appropriate setting for the patient. Response rate was near 99%.

The consultants estimated that 51% were not suitable for community placement, 19% would need nursing home facilities, and 29% could be discharged to community settings. Out of this latter 29%, 13% were for group homes supervised by trained staff, and 12% for hostels or group residences staffed by private owners or a warden; only 3% were envisaged in cluster flats, and less than 1% in independent accommodation.

Our consultants estimated a greater need for facilities staffed by professionals than was found in the Glasgow survey. The discrepancy may stem from at least two sources. Firstly, our consultants' perception may be more conservative in terms of the amount of supervision required by the discharged patients. However, the estimates of potential discharge rates were very similar. Secondly, the residential services practices may differ. For example, one of us (AL) trained in London and saw some "residence staffed by non-professional personnel" actually staffed by trained psychiatric nurses (paid as non-professional).

It will be interesting to compare our experience with the Scottish one in the years to come. Attention should be paid to carefully describing the type of accommodation and the level of staffing. In the end, only actual trial of discharge and follow-up to assess outcome will indicate how many sheltered housing places with professional staff are required and what resources need to be committed to this end.

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Affective 'switch mechanisms'

SIR: We fear Mobayed (*Journal*, June 1989, **154**, 884) has got hold of the wrong end of the stick. In our paper (*Journal*, January 1989, **154**, 48–51) we referred to our previous results which showed that SAM enters the CSF, is linked with CSF 5HIAA and folate metabolism, and influences prolactin. We not unreasonably thought that anything which influences prolactin and CSF HVA might have an effect on the dopamine system. Nowhere have we excluded an effect on serotonin also.

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The opiate prescribing debate continued

SIR: Hill (*Journal*, June 1989, **154**, 888–889) may well consider prescribing a tot of best Scotch whisky to an alcoholic, if it would stop his patients robbing someone and paying a gangster for adulterated meths.

It is important to realise that any response, including continuing as before, is a policy which must be evaluated, otherwise clinging to it is purely emotive, especially if continuing as before sees a relentless increase in the drug problem. This is just what has happened in America since the 1920s and in western Europe since the 1960s.

Our own appraisal found that, paradoxically, making drugs available in a controlled fashion *reduced* the problem (Marks, 1987; *Lancet*, 1987). It therefore seems reasonable to conduct a further experiment on the lines of the Mersey Clinics' experiments in Widnes and Warrington to see if our findings can be repeated or refuted.

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References

MARKS, J. A. (1987) Treatment of drug addicts. *British Journal of Addiction*, **82**, 813–814.

LANCET (1987) Management of drug addicts. *Lancet*, *i*, 1068–1069.

Case conference correction

SIR: I wish to dissociate myself from some of the remarks attributed to me in the case conference report by Howells & Beats (*Journal*, June 1989, **154**, 872–876). The second sentence of what I am alleged to have said is ungrammatical, inaccurate and offensive in tone. As the conference was not tape recorded I cannot quote my exact words, but I do recall commenting on the problem of alcoholism in the USSR and on media reports of Soviet airforce personnel consuming aircraft de-icing fluid (N.B. *not* engine fluid). However, I did not and should not have intended to put my points in such terms as were published. I sincerely hope they will not have caused offence.

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Distress caused by miscarriage

SIR: Milner (*Journal*, July 1989, **155**, 127) raises the issue of the amount of distress caused by miscarriage. Research shortly to be published in this *Journal* (Friedman & Gath, 1989) indicates high levels of distress in a group of women one month after miscarriage. In a series of 67 women, 48% PSE cases and two cases of self-harm not known to the medical profession were found. Another paper (Friedman, 1989) discusses the dissatisfaction of patients with their management and the problems of caring for this group of patients.

I agree with Dr Milner on the need for doctors and nurses to be more aware of this distressing condition, and that quite simple intervention may be effective in alleviating the considerable emotional turmoil caused.

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References

FRIEDMAN, T. & GATH, D. (1989) The psychiatric effects of spontaneous abortions. *British Journal of Psychiatry* (in press)

FRIEDMAN, T. (1989) General practitioners' management of miscarriage. *Journal of the Royal College of General Practitioners* (in press).

CPK levels and neuroleptic malignant syndrome

SIR: I was interested to read Maharajh's letter (*Journal*, June 1989, **154**, 885–886), as our District Biochemist, Mr G. Trevis, and I have recently started looking at the interpretation of CPK levels (including isoforms of MM isoenzymes) in the face of many variables. For example, elevated levels have been found in acute cerebral disorders, head injury, alcohol excess, muscle diseases, after oral neuroleptics, and in renal, cardiac, or thyroid dysfunction.

Some years ago there was considerable interest in elevated levels of CPK in patients with acute psychosis, and now more recently in raised CPK in neuroleptic malignant syndrome (NMS). I would suggest that a diagnosis of NMS should depend far more on clinical examination than finding a raised CPK. It has been suggested that the raised levels in acute psychotic patients may well be due to increased motor activity (Goode *et al*, 1979) or even intramuscular injections, but a study by Kumar (1984) looking at levels of CPK in schizophrenics and their first-degree relatives compared with normal controls found not only significantly raised CPK levels in the patient population but also in the first-degree relatives compared with normal subjects. The phenomenon of malignant hyperthermia has much in common with NMS, and again has been associated with increased CPK levels, and at one time it was thought that a raised level may predict a susceptibility to malignant hyperthermia, although this was subsequently refuted (Paasuke & Brownell, 1986).

Finally, I note that Dr Maharajh questions what the levels of CPK may be in black psychotic patients without NMS. Earlier work (Meltzer & Holy, 1974) has suggested that there are sex–race differences in serum CPK activity, levels being highest among black males and lowest among white females, and more recently a study by Gledhill *et al* (1988) confirmed that black males had higher CPK levels than white males.

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References

GLEDHILL, R. F., VAN DER MERWE, C. A., GREYLING, M. *et al* (1988) Race–gender differences in serum creatine kinase activity: a study among South Africans. *Journal of Neurology, Neurosurgery & Psychiatry*, **51**, 301–304

GOODE, D. J., MELTZER, H. Y., MORRETTI, R. *et al* (1979) The relationship between wrist monitored motor activity and serum CPK activity in psychiatric in-patients. *British Journal of Psychiatry*, **135**, 62–66.

KUMAR, A., UPADHYAYA, G. L. & TRIVEDI, J. K. (1984) Serum CPK levels in schizophrenics and their first degree relatives. *Indian Journal of Physiology and Pharmacology*, **28**, 128–132.

MELTZER, H. Y. & HOLY, P. A. (1974) Black–white differences in serum creatine phosphokinase (CPK) activity. *Clinica Chimica Acta*, **54**, 215–224.

PAASUKE, R. T. & BROWNELL, A. K. (1986) Serum creatine kinase level as a screening test for susceptibility to malignant hyperthermia. *Journal of the American Medical Association*, **255**, 769–771.

Paradoxical intervention

SIR: Macdonald's letter (*Journal*, June 1989, **154**, 883) has prompted me to read the case report of use of paradoxical intervention in a ritualist woman by Adshead *et al* (*Journal*, December 1988, **153**, 821–823) and put pen to paper. While paradoxical strategies are useful and effective in the treatment of many problems from thumbsucking to schizophrenia (Seltzer, 1986), either as an adjunct to other treatments or on its own, unscrupulous or erroneous application may lead to disastrous consequences for the patient, the therapist, and their therapeutic relationship. Adshead *et al* would see themselves as lucky at just feeling uncomfortable to "maintain a firm sceptical stance" and to face the disruption of therapeutic relationship if they knew that some physicians in ancient China (as early as 280 BC) even got killed for treating (successfully!) their emperors with paradoxical strategies (Wang, 1986).

As a non-specific method, paradoxical strategies can be applied to any number of neurotic and psychotic conditions irrespective of the aetiological basis. It acts through three main mechanisms: (a) breaking the vicious cycle of symptom-formation by reducing the performance anxiety, e.g. in the treatment of insomnia and sexual dysfunction; (b) eliminating resistance against therapeutic changes by putting the patient into a therapeutic double-bind no-lose situation so that the patient is held responsible for the control of symptom and the change, e.g. paradox used in hypnosis (Ericksonian) and paradoxical psychotherapy; (c) providing a new frame of reference to look at the pathological context, distancing the patient from the symptom by the use of humour, ridicule, sarcasm, and absurdity. Paradoxical intervention is appealing to the person's integrity and depends on the therapist's accurate and intuitive understanding of the psychopathology and assessment of the patient's resources. One of the prerequisites of paradoxical intervention is the intense relationship between the therapist and the patient rather than the content of the intervention (Seltzer, 1986).

Dr Adshead *et al*'s case report serves well to demonstrate what can go wrong with the use of paradoxical intervention. Instead of putting the patient into a therapeutic double-bind, no-lose situation, Dr Adshead has trapped her into a pathogenic double-bind, damned-if-you-do-it-and-damned-if-you-do-not position by the anti-exposure treatment of "Do not practice exposure". She was doomed either to comply with the psychiatrist's words and refrain from practising exposure, which was effective in the beginning, and probably stay on with her symptoms for another 10 years, or to disrupt the therapeutic alliance and mobilise other resourses to help herself. Luckily this woman had enough integrity to seek help from the nurse therapist (angel-delegate) and another psychiatrist and finally gained improvement. As for the psychiatrists (the devil-delegate in this case), maybe they can escape from their self-inflicted no-win predicament by changing their anti-exposure treatment to "Do not practice exposure if you don't really want to change". Whatever the patient's choice or outcome turns out to be, the psychiatrists will not be confronted with hostility and ungratefulness from the patient.

Another comment on the case report is that despite the prominent depressive features and the possibility of an underlying affective illness giving rise to the obsessive/compulsive symptoms, and despite the interesting coincidence of a relapse of symptoms at the time of returning home on discharge or weekend leave, with the couple refusing marital therapy and denying any relationship problem while frequent arguments could be seen when the husband was involved in the treatment scheme, the authors were ascribing the failure of treatment to the patient's non-compliance instead of looking into other psychosocial factors relevant to the perpetuation of the symptoms.

Finally, the main therapeutic techniques responsible for the favourable outcome in this case seem to be the exposure and response prevention (or maybe the 'support' by the other psychiatrist?) instead of the paradoxical intervention. Giving unjustified credit to the paradoxical intervention may be doing more harm than good to our understanding and mastery of this psychotherapeutic technique. Cautious evaluation and clear rationale may be the best guiding principles for the application of this effective and flexible armament in psychotherapy.

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References

SELTZER, L. F. (1986) *Paradoxical Strategies in Psychotherapy*. New York: John Wiley & Sons.

WANG, M. Q. (1986) *Psychotherapy in Traditional Chinese Medicine* (in Chinese). Szechwan: Chung King.

Psychiatric despotism?

SIR: Returning from Hungary, that most oriental and Asiatic of European countries (in every locality there is a thoroughfare named in honour of Attila), I find two Hungarians, Imre Karacs in the *Sunday Times* and Thomas Szasz in the *Journal* (June 1989, **154**, 864–869), using the terms "Asiatic despotism" and "oriental despotism" respectively, to describe that of which they do not approve.

Is this Hungarian self-hatred or racism? Szasz would have us believe that occidental despotism is made more acceptable by what he calls Judeo-Christianity. But Moses, Paul, and Jesus and all his disciples were worthy oriental gentlemen!

Stalin, Hitler, Mussolini, Franco and Rudolf Hoess (Commandant at Auschwitz) were all Christians. Not one was excommunicated. Two, Stalin and Hoess, studied at religious seminaries and had considered taking Holy Orders. The only oriental to compare with this European class in recent times is Pol Pot.

I hope that the Editor will guard against any hint of racism creeping into the *Journal*.

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Anorexia nervosa and Chinese food

SIR: From my personal experience both here in Hong Kong and in the UK, I agree with the paper by Lee *et al* (*Journal*, May 1989, **154**, 683–688) that there are far fewer cases of anorexia nervosa in the Chinese.

However, I think the exact reason why this is so is still far from clear. Dr Lee *et al* cited three cases and concluded that socio-cultural factors are the most important. Three years ago, I arrived at the same conclusion, although by a common-sense approach from the discussion I had with my tutor in the Maudsley hospital. Then, as now, I think that at least three other factors are also important. The first is the immense importance attached to food and eating in the Chinese culture. There is a Chinese proverb saying that "of all things in life, food is the most important". Indeed, to the Chinese, food is a bit like God, paramount and ubiquitous. Secondly, Chinese food is delicious. I think it is simply so delicious that one can hardly resist eating it. Thirdly, it is the Chinese custom to eat meals with their family. Everyone is expected to eat a certain amount, and it is quite difficult to go unnoticed if one departs from one's usual quantity. There is thus always a social pressure from the family for people to conform in order to avoid undue concern to other family members.

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Oculogyric crises and schizophrenia

SIR: I found the paper by Chiu (*Journal*, July 1989, **155**, 110–113) very interesting. I would like to report a further case.

Case report: Miss M had a long-standing schizophrenic illness. Eight years ago, at the age of 31, she was admitted 4 weeks after a reduction in dose of depot zuclopenthixol followed by increased frequency of auditory hallucinosis. This consisted of multiple voices in the second or third person. The episodes would last from 1 to 24 hours. Unless very mild, they were associated with oculogyric crisis associated with dysphoria. A typical episode would start with auditory hallucinosis, increasing in severity and becoming associated with oculogyric crisis, and finish as auditory hallucinosis alone, dying away. During the oculogyric crisis, the eyes were deviated up or up and to the right. Pursuit eye movements laterally and downwards were possible but impersistent, and associated with flickering of the eyelids. Bringing the eyes down to the normal position voluntarily improved the auditory hallucinosis. Convergence was not possible. The right pupil was minimally larger than the left, and reacted more sluggishly to light. The only other abnormality on physical examination was mild postural hypotension. As well as zuclopenthixol, she was also being treated with chlorpromazine and an anticholinergic. Some further anticholinergic medication parenterally produced temporary improvement. An increased dose of chlorpromazine produced complete disappearance of the oculogyric crisis over 12 hours and of the auditory hallucinosis over 24 hours. She continued to show de Clérambault's syndrome, believing that the Prince of Wales had intentions towards her despite his impending marriage.

The cases reported suggest that the association of oculogyric crisis and auditory hallucinosis is not fortuitous. The relative contribution of disease and drug-induced disorder to the phenomenon is difficult to elucidate now, because the use of neuroleptic medication is nearly universal in schizophrenic illnesses. Strong conjugate upward rotation of the eyeballs, lasting for hours at a stretch with constant rapid flickering of the eyelids, was reported in schizophrenia in the pre-neuroleptic era at the time when oculogyric crisis was first being described in epidemic encephalitis (Farran-Ridge, 1926). Thus oculogyric crises may have been a feature of schizophrenic illness before the introduction of neuroleptic medication. They may have been given other descriptions, such as 'mannerisms' (Rogers, 1985). If they were part of the disease process in some cases, this would make an association with other features of the disease process such as auditory hallucinosis more understandable. Medication obviously makes a significant contribution to the expression of both dystonic eye movements and hallucinosis, as in this case. The relative contribution of specific neurotransmitter disturbances to the oculogyric crisis is difficult to establish. Increase in either anticholinergic or anti-dopaminergic medication had a beneficial effect in the case reported.

Auditory hallucinosis in association with oculogyric crisis has only rarely been described, and then following encephalitis (Rosner, 1942). Even here it was rare. In Jelliffe's exhaustive summary of all reported cases of oculogyric crisis after epidemic encephalitis up to 1928 there was not a single case of such an association (Jelliffe, 1929). In schizophrenia this association has not been described before Chiu's report. This may be because of the paradoxical association between a resumed drug-induced disorder and one of the symptoms the drug is supposed to treat. In the case I report, the oculogyric crisis has been previously noted but described as hysterical, just as were the earliest cases of oculogyric crisis after the onset of epidemic encephalitis.

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References

Farran-Ridge, T. (1926) Some symptoms referable to the basal ganglia occurring in dementia praecox and epidemic encephalitis. *Journal of Mental Science*, **72**, 513–523.

Jelliffe, S. E. (1929) Oculogyric crisis as compulsion phenomena in post-encephalitis: their occurrence, phenomenology and meaning. *Journal of Nervous and Mental Disease*, **69**, 59–68, 165–184, 278–297, 415–426, 531–551 and 666–679.

Rogers, D. (1985) The motor disorders of severe psychiatric illness: a conflict of paradigms. *British Journal of Psychiatry*, **147**, 221–232.

Rosner, A. A. (1942) Unit reaction states in oculogyric crisis. *American Journal of Psychiatry*, **99**, 224–228.

Caution about sorcery

Sir: Keshavan *et al* (*Journal*, February 1989, **154**, 218–220) discuss the role of sorcery in the aetiology of psychopathology in rural India. I would like to discuss a case which acts as a caveat when looking for such explanations in the illnesses of recent immigrants to the United Kingdom.

Case report: A 28-year-old married Ghanian lady was admitted with a 3-month history of increasing estrangement from her husband and a week's history of mutism and not eating. Her husband reported that they had had an arranged marriage in Ghana four years previously, but that his wife had not joined him in England until two years later. He felt their marriage to be happy and without problems.

On examination she was dehydrated, but also approximately 28 weeks pregnant. She was initially mute, and was only persuaded to eat and drink with great difficulty. A diagnosis of depression was eventually made and a course of ECT was given, to which she made a good response.

The lack of information about our patient encouraged speculation as to the role of specific sociocultural factors in the aetiology of her illness. We felt that there was particular significance in the fact that she would not discuss and then denied her pregnancy. We discovered that there are traditional Ghanian beliefs leading pregnant women to think of their forthcoming child as a danger to themselves both physically and spiritually. Risks are much greater if the husband is not the father of the child; it is said that "adultery spoils the pregnancy", and it is felt very unlikely that such pregnancies will be safely delivered (Field, 1960).

These ideas led us to consider illegitimacy and worries about the pregnancy to be of major aetiological significance. However, when discussed with the patient prior to the course of ECT they did not elicit any response. The successful resolution of her illness allowed the patient to tell us that such views were very old-fashioned and now rarely believed. The problems she faced were much better understood in the context of isolation, a difficult marriage, and feeling very homesick.

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Field, M. J. (1960) *Search for Security*. London: Faber and Faber.

Benign intracranial hypertension and repeated self-mutilation

Sir: It is surprising that a void exists in the literature concerning the subject of psychiatric morbidity and benign intracranial hypertension, other than mentions in passing of feelings of subjective tension and discussions of the mental impairment suffered in children with the disorder.

Case report: Miss A, a 23-year-old unemployed single mother living alone with her child, was first seen as an overdose referral, having been admitted to the General Hospital following ingestion of 20 temazepam tablets to "relieve" the tension in her head. A careful history revealed no ideational or biological aspects suggestive of depressive illness.

On reflection she felt that she had never been happy even as a child, and that although there had been no specific traumas in her early life she had been shown little affection by her parents. At the age of 15, apparently unrelated to any social difficulties at the time, she began to experience feelings of extreme tension which she found difficult to explain in detail, but described as being not exactly pain but more a feeling of pressure building up to such a pitch that she felt as if her head was going to explode. The only way in which she was able to relieve this tension was by self-mutilation, and over the three years between the ages of 15 and 18 she made repeated superficial slashes to her forearms and also clawed at her face on several occasions with superficial injury resulting. All of these manouevres were efficient in relieving tension, but she was ashamed of her actions, talked about them little to family or friends, and always completed the acts when alone. At the age of 18 intractable headaches developed. An appointment with a neurologist was arranged, and benign intracranial hypertension was diagnosed on the basis of papilloedema, CT scan, and lumbar puncture, and was subsequently treated with serial lumbar punctures.

Following this procedure, both the headaches and feelings of tension disappeared. Despite a fairly turbulent life pattern over the subsequent few years no recurrence of the tension or headaches developed until the age of 22, when the subjective feelings of tension returned and the self-mutilating behaviour recommenced. Over the past few weeks she has suffered headaches of increasing severity, and she once more has papilloedema on clinical examination.

She is currently being investigated and treated for recurrence of benign intracranial hypertension by the neurologist.

Our case could well be described as being typical of someone engaged in repetitive self-mutilation, as is shown by a recent large study (Favazza & Conterio, 1989). The psychiatric literature on the subject of benign intracranial hypertension is sparse, but feelings of tension are described in most of the comprehensive neurological texts (Vinken & Bruyn, 1982).

In this particular case it is tempting to propose a model wherein subjective feelings of tension precipitated by benign intracranial hypertension induced self-mutilating behaviour, a proposal which would receive support from the temporal relationship with the symptom complexes and which must lead to the speculation that perhaps benign intracranial hypertension may be an underlying, undiagnosd factor in a larger proportion of patients with repetitive self-mutilation than has so far been realised. It would seem essential to perform a funduscopic examination when reviewing these patients.

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References

FAVAZZA, J. R. & CONTERIO, K. (1989) Female habitual self mutilators. *Acta Psychiatrica Scandinavica*, **79**, 283–289.

VINKEN, P. J. & BRUYN, G. W. (1982) *Handbook of Clinical Neurology*, **42**, 740.

A HUNDRED YEARS AGO

Dr Brown-Séquard's hypodermic fluid

The extraordinary statements made by Professor Brown-Séquard as to the efficiency of hypodermic injections of fluid expressed from the testicles of young animals in senile debility have been to a certain extent confirmed by M. Variot, who made a communication to the Société de Biologie on June 29th. The patients chosen were debilitated men, aged 54, 56 and 68 years respectively, and they were not informed of the nature of the treatment adopted. In all three cases the injections were followed by general nervous excitement, increased muscular power, and stimulation and regulation of digestion. M. Brown-Séquard said that M. Variot's observations disposed of the objection that the results he had observed in himself were due to "suggestion".

Reference

British Medical Journal, 6 July 1889, 29.

Research by Henry Rollin, Emeritus Consultant Psychiatrist, Horton Hospital, Surrey

British Journal of Psychiatry (1989), **155**, 572–583

Book Reviews

Editor: Sidney Crown

Birth of a Self in Adulthood. By DOROTHEA MCARTHUR. New Jersey: Jason Aronson Inc. 1988. 227 pp.

The thesis of this book is that borderline patients are individuals whose development is prevented at any stage (although the focus is largely on the adult) by a variety of 'commands' (twelve maternal and eight paternal commands are listed) whose ultimate message is to "stay at home and serve as an extension of their parents' life". The emphasis is on the mother's commands, those of the father tending to be both complementary and supportive to those of the mother. The idea of 'impinged upon individuals' in need of appropriate interactions conducive to healthy growth is preferred to that of 'borderline pathology'. The healthy interactions referred to are the stuff of 'permissions', the benign counterparts of the malignant 'commands'. The severity of pathology is proportional to the preponderance of commands over permissions. It is suggested that the therapist's awareness and explanation of these commands, together with the provision (sometimes quite directively) of the appropriate antidote (permission), can significantly shorten the duration of therapy.

The book is not without virtue, and I value the enumeration of the maternal commands in chapter II, the core of the book. However, at the end of it I was left without a clear sense of what the author means by 'borderline'. It is unclear whether, in her view, all borderlines are 'impinged upon' or whether there are other routes to these states of mind. Although the introduction promises consideration of both the 'external living parents' and the 'intrapsychic parents', there is no real consideration of the latter, and no consideration of the mechanism which makes the individual vulnerable to the former. Indeed, there seems to be a conspicuous lack of attention to any intrapsychic dynamics such as this would imply, and no discussion of the dynamic issues which make work with severe pathology so problematic. There is, for instance, no mention of the superego, of the narcissistic character formation, of the role of envy or aggression. Perhaps more damning is the absence of any acknowledgement of systems theory, which is the theory which comes closest to the model the author is suggesting. Finally, many would agree that without addressing 'the system' through the patient it is often impossible to achieve any result (although this is not confined to 'borderline' conditions), but it is usually important early on in an analysis or therapy, often in the establishment of the therapeutic alliance, and as an important preliminary to establishing the intrapsychic pressures on a patient to maintain their allegiance to the system. It is rare for this work to take place within the relatively short period of two years suggested by the author. Perhaps, however, we are not talking about the same population.

The author clearly feels that she has been therapeutically successful with a difficult class of patients, and she offers an important corrective to a literature which sometimes gives too little weight to environmental issues both in the past and in the present. Perhaps she fails to convey her thesis cogently because of the readership she is aiming for: both patients and psychotherapists in training. The former will not be helped to look for their own contribution to pathogenesis; the latter will find neither argument (barely any of the many references illuminate the text) nor technical direction.

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Psychotherapy of the Disorders of the Self: The Masterson Approach. Edited by JAMES F. MASTERSON and RALPH KLEIN. New York: Brunner/Mazel Publishers. 1989. 480 pp. $39.95.

This volume is divided into five topic areas, covering the essentials of theory, the scope and techniques of psychotherapy using the Masterson approach, and other important areas such as countertransference, supervision, and the use of drugs in the treatment of personality disorders. It is a collection of contributions from therapists trained in the Masterson approach working both in New York and California.

Masterson introduces the volume with a résumé of his development, which goes hand in hand with the development of his ideas in treating personality disorders. Over the past 32 years the Masterson approach has evolved through his work with children, adolescents, and adults. Combining the object relations theory with the developmental model based on the work of Margaret Mahler, Masterson offers a theoretical framework from which a special form of psychotherapy has evolved.

Integrating Kernberg's ideas on the four stages of development of normal internalised object relations, Margaret Mahler's concepts of separation-individuation, and the self theorists' study of the individual's progress to libidinal self constancy, Masterson has developed the concept of the 'real self'. This is the integration of capacities such as separation, individuation, and experience of the self with or without others into a personality structure.

Impairments in the real self are due to nature, nurture and fate. Nature here consists of constitutional or genetic defects, 'nurture' refers to maternal libidinal unavailability, and fate is defined as "any event that diminishes the mother's libidinal unavailability or interferes with the child's individuation in the first three years of life".

Even though other personality disorders are mentioned, the authors concentrate on the borderline and narcissistic personality disorders. The intrapsychic structure of the narcissist is due to an arrest at the practising subphase of separation-individuation, composed of two object relations fused part-units – "the grandiose self-omnipotent object fused part unit and an underlying pathological aggressive or empty object relations fused-unit." The borderline personality structure is thought to be due to a developmental arrest in the critical rapprochement subphase of separation-individuation. The split intrapsychic structure that ensues is characterised by rewarding and withdrawing object relations part-units, each with its component self and object representation. In essence, Masterson views personality disorders as a defence against the activation of the real self and the emergence of abandonment depression.

The therapeutic technique uses the theoretical concepts in identifying this false defensive self, challenging the patient to give it up and working through the abandonment depression. With borderline patients the principal technique advocated by Masterson is that of confrontation, which is defined as "a therapeutic intervention that demonstrates to the patient a resistance or defense against the operation and expression of the healthy ego or emerging real self." For the narcissistic disorders Masterson emphasises the use of interpretation of the patient's "microscopic" vulnerability to injury as a primary therapeutic technique.

This volume is full of examples of the techniques used, and the authors tackle in a clear and compelling way the issues of transference and countertransference in their struggle with such difficult patients. The correlation between the clinical phenomena encountered and the theoretical concepts accounting for their development are lucidly outlined.

There is much to be learnt from this book for those involved in the psychoanalytic psychotherapy of borderline and narcissistic patients.

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Psychodynamics and Cognition. Edited by MARDI HOROWITZ. Chicago: University of Chicago Press. 1988. 389 pp. £21.95.

Horowitz points out that the existence of unconscious systems for organising meaning and guiding information processing is a relatively recent scientific discovery. Mesmerists, hypnotists, and then psychoanalysts all described the phenomena, but presented different explanations. More recently, cognitive psychologists have shown an interest in these processes. Both cognitive and psychodynamic science may deal with processes involved in unconscious defences aimed at reducing potential anxiety, but whereas the psychodynamic approach asks the question "why?", the cognitive approach suggests "how". In this way, a bridge can be formed between psychodynamic and cognitive psychology.

According to Horowitz, "Psychodynamics concerns configurations in interaction between wishes, the threats anticipated to arise if the wishes are exposed, and the regulatory processes used to cope with, or defend against this conflictual situation." Although Freud did attempt an account of how repression took place, using his energy economic model and the notion of cathexis and decathexis of representations – his early "Project for a Scientific Psychology" being a sophisticated cognitive psychology – on the whole, analysts have not concerned themselves with models of how mental defence takes place. Melanie Klein, for example, described detailed defence mechanisms constituted by unconscious fantasy. In her view, the defence *was* the fantasy – she did not recognise the need to describe structure and process as well as, and as distinct from, content of the mind.

The modes of unconscious information processing have begun to be addressed by cognitive psychologists in ways that permit links to psychodynamic theory. On the whole, however, theories of cognitive psychology are often tested using emotionally neutral stimuli, or contrived laboratory situations which do not approximate the emotionally charged interactions of real relationships, or of the analytic consulting room, and therefore do not adequately represent the mind in conflict. The papers in this collection work towards a more clinically relevant cognitive psychology.

Several papers address Luborski's 20-year research into the phenomenon of momentary forgetting during the analytic session. Luborski finds that when numerous instances are studied, a consistent contextual pattern is discovered for each patient, always involving the activation of the patient's particular "core conflictual relationship theme" in relation to the analyst. Baars discusses this phenomenon in terms of an interesting model of 'resetting' of a 'conscious global work-space' due to competition between incompatible contexts. He uses a 'publicity metaphor' to describe how conscious awareness can provide a kind of systematic broadcasting of a message to many different areas of the mind – like a politician or a scientist gaining access to the media. This notion of 'publicity' is the flip-side of Freud's censorship metaphor, which describes how disturbing information is confined to isolated parts of the mind and kept incommunicado. Only one message can appear on the consciousness screen at once – hence, while publication is adaptive in gaining the attention of broad areas of the mind, conscious processes are serial, slow, and inefficient compared with unconscious processes.

The mixing of clinicians and academic theorists in this book is not always smooth. Baars, for example, spoils his otherwise convincing paper with his bizarre suggestion that as a research strategy a therapist might deliberately "overload the patient's immediate memory by asking him/her to say three sentences about the three most important things on his mind." Nevertheless, the authors persuasively argue the case for a psychodynamic cognitive science. There are some interesting general suggestions as to possible lines of enquiry and theory. Overall, however, this clinician is left very much with the impression that there is more promise than substance so far in this endeavour.

PHIL MOLLON, *District Psychologist and Adult Psychotherapist, Lister Hospital, Stevenage, Herts*

Countertransference Triumphs and Catastrophes. By PETER L. GIOVACCHINI. London: Jason Aronson. 1989. 335 pp. £23.50.

Countertransference can be defined, in its broadest sense, as the therapist's feeling response to the patient. Giovacchini's book has much to offer any clinician who practises psychotherapy or analysis. Although what he writes is not new, at least in British schools of depth analysis, he writes well on the subject, and engages interest in the pitfalls awaiting the therapist who is not monitoring his or her countertransference. Some of the many examples are extreme – one is of a patient who shot his therapist dead. However, the exploration is always interesting.

Giovacchini is a Chicago-trained psychoanalyst, and thus from a traditional American Freudian analytic background. However, he has absorbed and pays tribute to the British objects relations school, and quotes Klein and Winnicott frequently. At times he misinterprets Winnicott, as when he describes children being treated by their parents as transitional objects. By this he means children who are used in various ways to enhance parental narcissism. This is a misuse of Winnicott's term "transitional object".

Following an opening chapter, "The therapist's contributions to the course of therapy", the book is divided into three parts. The first is called "Countertransference and disruption". Giovacchini describes the ubiquity of countertransference, and points out that an apparent absence of it is an indication of a problem. In writing of disruption of the process he treats of ways in which patients may provoke countertransference responses which, acted out in subtle ways, destroy the treatment.

The second, and by far the largest, section of the book is entitled "Countertransference in specific psychopathological constellations". Although his thesis in general seems to be that the more primitive the psychic organisation of the patient, the more intense the countertransference, the author also argues for the difficulties in countertransference with depressed patients. He suggests, as a result, that depressive disorders will cause us to revise current attitudes to psychopathology and treatment.

The short final section is on "Technical treatment problems". Giovacchini seems quite often to favour a direct use of the countertransference, i.e. the therapist describing his feelings to the patient so that they can look together at what has gone on. He is fairly scathing about the idealisation involved in the use of the term 'classical psychoanalysis'. By mentioning this I do not mean to imply that his work with patients, as he describes it, is unanalytic. What I do feel, however, is that his theoretical framework does not come through clearly.

The strengths of this book lie in the full examples – it is a very clinical book – and in Giovaccini's commitment to exploration of the ever-present phenomenon of countertransference. As he points out at the end, "The recognition of its effects and its role in the treatment interaction has broadened the scope of psychoanalytic treatment and has made the analytic interaction a human and mutually enriching experience".

NICOLA BLANDFORD, *Senior Registrar, Department of Psychotherapy, Cambridge*

Problems and Solutions in Marital and Family Therapy. By JOHN CARPENTER and ANDY TREACHER. Oxford: Basil Blackwell. 1989. 271 pp. £9.95 (pb), £29.50 (hb).

This is a useful book, which should be recommended to beginning therapists. It contains much good common sense, and many practical tips. The first three chapters set out the basic model, which is principally borrowed (with due acknowledgment) from the 'Brief Therapy Project' at the Mental Research Institute in Palo Alto. The emphasis is on focusing on solutions, not problems, and on developing a therapeutic alliance. Chapter four is on the engagement of young children in therapy, and chapters five and six are on dealing with the specific problems of secrets in therapy, and of violence in the family. Chapters seven and eight are on the authors' approach to the management of what they call 'stuckness' in the therapeutic and supervisory systems. The final chapter is about managing endings in therapy.

The first chapter challenges the concept of resistance in therapy. The authors make some valid points, but although it is true that a few schools do, or did, use the concept of resistance to describe an almost adversarial therapy, in the current climate of opinion I suspect they may be tilting at windmills. The description of 'contract building' is quite useful, but would gain weight if they referred to some of the considerable body of work which has been done on this subject. Many therapists would strongly support their accent on the relationship between therapist and family. This chapter could be misinterpreted, however, as implying that there is a simple schema which can allow the therapist or the family to avoid very painful choices.

Chapter two provides common sense on convening a session. It describes the obstacles to be overcome in the various settings (clinical and statutory) in which therapeutic work (not just 'therapy') has to be done. This and the previous chapter do a good job of demystifying the therapeutic process, but above all the attention to the wider social, political, and racial/cultural issues as they affect both the family and therapist is excellent.

The chapter on the inclusion of young children is disappointing. It gives good reasons for including young children and some pointers about how to use their presence, but fails to tackle the question most newer therapists want help with: how do I find a language in which to talk to children without being patronising, and still be respectful to adults?

The chapters on secrets and violence are sensible and contain much good advice, as do chapters seven and eight.

The authors are quick to find models to criticise, but do not really say what the therapist needs to learn in order to become a good therapist. Their sensible and systematic approach sometimes fails to inform the reader that therapy (and life) includes confronting what may appear to be irrational, or alternatively broadening our perspectives of the rational. The reader might need to be reminded that he or she may have to make jumps in perception in order to help the family detoxify the irrational. This is a book which should be used by trainers.

ALAN I. COOKLIN, *89 Southwood Lane, London*

Man and Dog: The Psychology of a Relationship. By REINHOLD BERGLER. Oxford: Blackwell Scientific. 1988. 224 pp. £12.95.

To a certain extent our quality and enjoyment of life depend on the level of importance we attach to other people and other things. Relationships between human beings and animals form an extensive part of this world of meanings and values. In this text Bergler endeavours to examine the nature and significance of the relationship between man and dog and the effect it can have on people's lives. He presents scientific evidence to support the importance of dogs in improving the life of man and indicate how dogs could come to play an even more effective role in the future.

The book covers in detail the role of dogs in art and culture, the personality of dog-owners, and the role of dogs in medicine – for example, in the treatment and prevention of cardiovascular disorders. Bergler also examines to what extent animals have proved to be beneficial in the field of psychotherapy. We read about amazing results gained with autistic children, the old, the mentally ill, and the disabled.

This is a thoroughly fascinating book which should appeal to a wide readership – ranging from social workers, psychiatrists, and psychologists, to vets and, last but by no means least, the army of interested dog owners out there! At £12.95, this book should find itself on a variety of different bookshelves.

SARAH CONYERS, *Editorial Assistant, British Journal of Psychiatry*

Masculinity/Femininity: Basic Perspectives. Edited by JUNE MACHOVER REINISCH, LEONARD A. ROSENBLUM and STEPHANIE A. SANDERS. New York and Oxford: Oxford University Press. 1987. 364 pp. £28.00.

This excellent book provides some coverage of every area of study relevant to this highly contentious subject. It includes psychobiological, neuroscience, evolutionary, behavioural genetics, developmental, psychosocial, and cultural perspectives. Almost every chapter is followed by another commenting on the previous one, so that doubts, difficulties, or disagreements raised in one's mind are often immediately dealt with in the same volume. The emphasis is on exploring concepts and methodology and examining the problems and pitfalls of research.

There are at least three definitions of masculinity/femininity: behaviour typical of males or females; role expectations of males and females; and the qualities of one sex that attract the other. It is certainly not unidimensional; for example, 'feminine' little girls, who like pretty dresses and hair bows, can score highly on a 'masculinity' scale which emphasises the need for control, power, and dominance. The various definitions and concepts are kept carefully apart, and anyone who has simplistic ideas about the differences between males and females should suffer a rude awakening on reading this book.

Those who know this field may find it a useful revision, but will probably be familiar with its contents, at least in their own speciality, since the chapters are all based on papers from a conference held in 1984. The papers have, however, been revised and updated and there are a few more recent references.

The papers do not make easy reading, but it is well worth the effort in almost every case. I particularly enjoyed the fascinating and copiously illustrated chapter on masculinity and femininity in 'elaborated movement systems' (mainly dance).

CHARMIAN BOLLINGER, *Consulting Clinical Psychologist, The London Medical Centre; Honorary Therapist, Sexual Dysfunction Clinic, St George's Hospital, London*

A Dictionary of Kleinian Thought. By R. D. HINSHELWOOD. London: Free Association Books. 1988. 482 pp. £35.00.

In the last few decades there have been considerable developments within a number of clinical and theoretical psychoanalytic frameworks. Some of these advances have significant implications for clinical work with certain types of psychopathology and for our further understanding of aspects of normal and abnormal mental development, as well as aiding clarification of some of the complex issues affecting society.

The Kleinian school of psychoanalysis (one of three groups within the British Psychoanalytic Society) has made some of the more radical and controversial claims about aspects of mental life. These theories considerably diverge from, and enlarge upon, classical and ego psychology viewpoints. For example, Kleinians have long claimed that the infant has some primitive sense of itself from birth and can distinguish objects separate from itself. Furthermore, they define a variety of primitive and complex psychological mechanisms which they feel operate actively from the earliest days and weeks of life. They suggest that these: (a) protect the baby's mind from unbearable feelings and anxieties; (b) communicate these experiences; and (c) create conditions in which the early mental apparatus can develop (e.g. normal splitting).

Kleinians claim that these early mental mechanisms and their closely related fantasies remain potentially operative to varying degrees in all human beings throughout life, and that a fuller awareness of their existence throws considerable light on clinical conditions previously regarded as unamenable to psychodynamic treatment, e.g. various psychotic states, and narcissistic and borderline disturbances. Recent advances and infant research using other sources of data have given additional credence to some of the sophisticated mental capacities long claimed for infants by Kleinians.

However, there are many problems in communicating the complex ideas of the Kleinian school, both to those who have had different professional trainings within the mental health field and to other scholars.

Hinshelwood's *Dictionary* is a most welcome and timely edition to the now substantial Kleinian literature. The book is highly successful in its intention of being an accessible account of Kleinian and post-Kleinian concepts. Some of the leading Kleinian writers, including Klein, did not have the literary prowess of Freud, and in addition the concepts and processes that they delineated are often far from conscious, and therefore not part of everyday commonsense and verbal currency. The book should satisfy the serious enquirer who wishes to gain a clearer intellectual understanding of the phenomena Kleinians are describing, and the ways in which these ideas diverge from, or add to, other theories. However, eventual agreement or refutation of these ideas can only depend on the reader being prepared to expose himself or herself to extensive personal and clinical experience in which he will need not only the intellectual aspects of his mind.

The book is divided into two major sections. In the first part Hinshelwood takes, in chronological sequence, what he regards as 13 major areas to which Klein made significant theoretical contributions. He gives definitions of each concept, and then a brief chronology of the major writings on the concept. This is followed by detailed elucidation of the many facets of the topic and their elaboration by those who followed Klein. He also gives an account of criticisms and disagreements of the Kleinian concepts stemming from other schools.

The first entry is on Kleinian technique with both children and adults. The reader learns of Klein's growing conviction that interpretative response to the very young child's spontaneous play was most valuable in gaining further access to the child's unconscious life and to his central mental preoccupations and mechanisms. The technique aroused great controversy, and also the important question as to how much the clinical data was an artefact of the technique and of the types of interpretations that formed a central component of the technique.

The other major entries include entries on the Kleinian concept of unconscious fantasy, the paranoid schizoid and the depressive positions, and also a thorough exposition of the various concepts contained within the term 'projective identification'. This is an umbrella term that has received extensive evaluation in the last three decades. This book goes in some detail into the various ways in which many Kleinians feel that projective identification has helped to add to our understanding of other mental phenomena: (a) some exciting ideas about the way in which thinking comes about or is obstructed; (b) further understanding of symbolism and its failure, with great relevance to psychotic mechanisms; (c) the role of the primary object (parent) in its response to the child's projections; (d) the role of empathy; and (e) in psychoanalytically-based treatments, a much more central role for the examination of the counter-transference as a clinical tool for understanding the patient.

The book is excellently cross-referenced. For example, the five areas described above in relation to projective identification also each receive an extensive entry in their own right.

The second half of the book consists of about 170 general entries, in alphabetical order. These include a few brief biographies of key members of the Kleinian school, with short accounts of their main contributions. The latter are cross-referenced to separate entries in which the concept itself is discussed in greater depth; examples are 'omnipotence', 'symbolic equation', 'persecution', and 'reparation'. I found very few errors in the book, although there are occasional lapses into colloquial language which are surprising in an otherwise scholarly endeavour. Each section has an excellent list of references for the interested reader, and a full list of Kleinian literature appears at the end of the book.

I would recommend every psychiatric library to keep a copy of this book in its reference section, and I am sure many psychiatrists will need no encouragement to buy a copy for themselves. It is a book that can be easily dipped into, and on my bookshelf will go alongside La Planche & Pontalis's *The Language of Psychoanalysis* and the Hampstead Clinic's *Basic Psychoanalytic Concepts – Vols 1–4*, which perform similar functions for classical and ego-psychoanalytic theories.

The aims of the publisher would be well served if a cheaper paperback edition were to be produced in the near future.

BRIAN V. MARTINDALE, *Consultant Psychiatrist in Psychotherapy, Paddington Centre for Psychotherapy and St Charles Hospital, London*

Fugitives of Incest: A Perspective from Psychoanalysis and Groups. By RAMON C. GANZARAIN and BONNIE J. BUCHELE. Madison: International Universities Press. 1988. 117 pp. $25.00.

Despite the dramatic recent increase in awareness of childhood sexual abuse (CSA), suprisingly little has been written about the treatment of its long-term destructive effects. The available literature emphasises the application of short-term cognitive-behavioural and group therapies.

Group treatments have a clear rationale. Many adult victims of CSA experience intense guilt, shame, and an incapacitating sense of isolation. In a homogeneous therapy group the traumatic and isolating experience of CSA unites the members, promoting cathartic self-disclosure, and a new sense of feeling accepted and of belonging. Characteristic interpersonal problems can be scrutinised and modified *in vivo*, especially if there are male and female cotherapists. Although powerful, however, short-term group treatments cannot afford an opportunity for the development of enduring self-esteem and self-control in those who have been most damaged by CSA.

In this stimulating, if clumsily titled, small book Ganzarain & Buchele draw from their experience of conducting long-term analytic group therapy with women who were abused in early childhood, concurrently with independent individual psychotherapy – a model which has been applied successfully in the treatment of patients with characterological disorders. They describe lucidly the dynamic processes which are characteristic of the most severely disturbed victims of CSA. In chapters on the transferences, countertransferences, and patterns of acting out which characterise their treatment, attention is drawn to dynamics which can inhibit or destroy the therapeutic process unless understood clearly and handled effectively by the therapists. In a chapter entitled 'Survival of the self in incest victims', they present some compelling ideas about the impact of sexual abuse on the developing self of the child victim. This then provides a helpful framework within which to conceptualise the dynamic processes already outlined, although the authors' attempt to connect this to the phenomena of DSM–III post-traumatic stress disorder is redundant and misleading.

Most timely and useful are Ganzarain & Buchele's reminders that "recovery from the severe trauma of incest is a lifelong process", and that, even with therapeutic assistance, lasting change is accomplished only gradually. This books serves to emphasise that there is not a single universal treatment, and that therapeutic strategies need to be personalised in a way that permits the pace of self-disclosure, self-examination, and change to be determined by the patient's needs.

MIKE HOBBS, *Consultant Psychotherapist, Warneford Hospital, Oxford*

MCQs for the MRCPsych Part II (New Syllabus). By MICHAEL I. LEVI. Lancaster: Kluwer Academic Publishers. 1989. 85 pp.

SAQs for the MRCPsych Part II (New Syllabus). By MICHAEL I. LEVI. Lancaster: Kluwer Academic Publishers. 1989. 86 pp.

These two brief and well-presented books have been produced principally for candidates preparing for the new MRCPsych Part II examination. The first one consists of 400 multiple choice questions (MCQs), covering 17 clinical topics, with answers provided at the end of the book. The second book comprises 200 short answer questions (SAQs), half of which are devoted to the 'basic sciences', and half to clinical topics. Again, answers are provided at the end of the book. The range and distribution of the SAQs and MCQs are based on the specimen papers produced by the Royal College of Psychiatrists. Reflecting as they do the new examination format and syllabus, the arrival of these two texts is timely.

Although Levi provides in the introductory section of each book a few pointers on examination technique, the most fundamental principle is that the candidate should be well-prepared and conversant with his subject through reading and clinical experience. As is indicated in the Foreword to each book, these texts are intended only as useful adjuncts to such learning. They are opportunities for examination practice and formative self-assessment.

Levi has not provided explanations or references because he expects these books to be used in association with the three reference texts which spawned his questions and answers. His choice of parent texts is very acceptable: *The Oxford Textbook of Psychiatry* (Gelder, Gath and Mayou, 1986) for the MCQ items, and the *Examination Notes on the Scientific Basis of Psychiatry* (Dinan, 1985) and the *Examination Notes in Psychiatry* (Bird & Harrison, 1987) for the SAQs.

As a co-author of a book of MCQs I can testify to the difficulties involved in trying to generate a battery of questions and answers which are unambiguous, accurate, and at an appropriate level of difficulty. However, these are important touchstones against which such books have to be assayed. It is unfortunate, therefore, that there are lapses in Levi's books. In the MCQ one, although the items are generally of a high standard, the range of difficulty is rather inconsistent. Moreover, certain response options appear to be inappropriate. For instance, "neurasthenia" is given as a possible answer to the stem "Therapeutic factors in small group psychotherapy include", and for the stem "Behaviour therapy for general anxiety states include" the option "anxiolytic drugs" is offered. One can also contest the accuracy of some of the answers. For instance, can one make the absolute claim that with supportive psychotherapy "obsessional neuroses definitely improve"?

Similar issues arise in the case of the SAQ items. The range of difficulty is variable and, at times, the stems are vague, e.g. "List the factors associated with agoraphobia". Inaccuracies also creep into some answers. Levi reports that the prognosis of bouffée délirante is "good" but, to be more accurate, it has a "good immediate prognosis, but often relapses" (according to *The Oxford Textbook of Psychiatry*). Also, I doubt if the author really believes that "Complete readjustment [to bereavement] occurs several weeks after the onset of the mourning phase".

In summary, therefore, Levi must be applauded for trying to meet the needs of candidates facing a new curriculum and examination, and for tackling such a broad range of topics. He set himself a daunting task. There are weaknesses in each book but these do not outweigh their potential value to candidates, who need such examination practice, providing that they use the books in concert with the textbooks recommended by Levi as well as with other specialised books.

DAVID A. ALEXANDER, *Senior Lecturer, Department of Mental Health, University of Aberdeen*

The Nature and Treatment of Anxiety Disorders. C. BARR TAYLOR and BRUCE ARNAW. New York: The Free Press. 422 pp. $35.00.

This is a solid and workmanlike account of current knowledge and research activities in the field of anxiety. One author is a psychiatrist, the other a psychologist, and they have collaborated well in integrating the two approaches. Thus, in discussing theory, assessment, and treatment the authors discuss a broad sweep from speculation, opinion, and data from psychophysiology and pharmacology through to psychodynamic mechanisms.

As both authors work at Stanford University it is not surprising that anxiety disorders are discussed according to DSM–III conventions. Sometimes these conventions can be followed too slavishly; it is pleasant to be able to report that, while broadly accepting this approach, the authors are aware of its limitations and introduce concepts, such as those of chronic and existential anxiety, that are not covered by the existing classification.

A practical, straightforward approach is adopted throughout the text, and this would appeal to the practising clinician. Case histories and examples of treatment response are given liberally, and there are 50 pages of appendices that will be invaluable for those designing clinical programmes for treatment. Although there are many competitors in the field, this book will stay ahead of most of them because of its good sense and practical value. It is definitely worth having in the medical library and, as it is well priced, in many personal ones also.

PETER TYRER, *Early Intervention Service, St Charles' Hospital, London*

Resolving Resistance in Group Psychotherapy. By LESLIE ROSENTHAL. Northvale, New Jersey: Jason Aronson. 1987. 209 pp. $20.00.

The literature on group psychotherapy has mushroomed since Yalom's masterly text first appeared, and there has been a need for an account of some of the particular difficulties in working with this most complex of all the psychodynamic techniques. Rosenthal, who is Dean of Group Psychoanalytic Studies in New York City, is in a good position to address this task. His book is a scholarly review of the literature. Its summary of the subject is comprehensive, yet somehow uninspiring. It begins with a careful account of Freud's views on resistance in psychoanalysis, and proceeds to show how these were developed by his successors, and also how they came to be incorporated into the new field of group psychotherapy. It ends with an interesting discussion of how the countertransference may produce resistances in the group therapist that slow the progress of the group's work. This is a book which should be referred to by group therapists, but would be of less general interest to other psychotherapists.

PETER SHOENBERG, *Consultant Psychotherapist, Joint Department of Psychotherapy, University College Hospital and Middlesex Hospital, London*

The Prefrontal Cortex; Anatomy, Physiology and Neuropsychology of the Frontal Lobe (2nd edn). By JOAQUIN M. FUSTER. New York: Raven Press. 1989. 255 pp.

This is a second edition of Fuster's well-timed text on the prefrontal cortex, originally published in 1980. Psychiatrists have had an interest in the frontal lobes ever since the classic descriptions of the personality changes that occured to Phineas Gage after his frontal lobes were destroyed by an iron rod which passed throught his skull following an explosion. The sequelae of frontal lobe syndromes has continued to be investigated since that time, and many of the consequences of frontal lobe destruction have direct bearing on psychiatric practice. More recently, the extensive evidence that frontal lobe changes may be seen using modern imaging techniques in such common psychiatric conditions as schizophrenia has re-emphasised and rekindled the psychiatrist's necessity to understand this extensive area of the cerebral cortex.

Those possessing the first edition will want to know the extent to which changes have been made. The majority of these, while having relevance for clinical practice, do not directly bear upon it. Thus, many of the additions have had to do with the neurophysiology and neurochemistry of the frontal areas, much of which is derived from animal investigations. There is thus an additional chapter on neurotransmitters, and that on neurophysiology has expanded by some 40%. The chapter on human studies has been restructured, although there are very few references that date beyond 1980. The 1986 monograph by Stuss & Benson (*The Frontal Lobes*) is quoted liberally here, and there is a new section on imaging studies, which derives largely from the studies of cerebral blood flow, especially with PET technology. The author supports the data suggesting hypofrontality in schizophrenia, and is impressed by the increased metabolic rates noted in orbital prefrontal areas of obsessive-compulsive patients.

Like others who have tackled the issue of the frontal lobes, Fuster has his own theory of the function of the prefrontal areas. He discusses the principle of the indisoluble union of perception and movement, based on a neural hierarchy which possesses circular connective patterns forming the basis of the perception-action cycle of cognition. It is central to his thesis that the prefrontal cortex is critical in the temporal structuring of behaviour, co-ordinating in particular provisional short-term memory, anticipatory preparation, and control of interference of behaviour by suppression of external and internal disruptive influences.

For those who do not possess the first edition of this book, the second is refreshingly easy to read, and provides much valuable insight into our experimental knowledge of the prefrontal cortex. It is perhaps less clearly clinical than the monograph by Stuss & Benson, but can be viewed as complementary to it.

MICHAEL R. TRIMBLE, *Consultant Physician in Psychological Medicine and Raymond Way Lecturer in Behavioural Neurology, The National Hospital for Nervous Diseases, London*

The Schizophrenias. Edited by FREDERIC FLACH. London: W. W. Norton. 1989. 233 pp. £20.95.

The aim of this multi-author book is to update the reader on a wide range of issues. Its title is a declaration of the contributors' allegiance to the concept of schizophrenia as a group of heterogeneous disorders. Appropriately, the first chapter is by Manfred Bleuler, who gives a lucid distillation of a lifetime of research and careful observations of the course and outcome of schizophrenia, with brief discussions of the criteria of recovery and the changes in prognosis in recent decades. The chapter is a masterpiece.

Andreasen reviews the historical development of the concept of schizophrenia, with Kraepelin as the starting point, and she raises some of the dilemmas in establishing a system of subtyping. A summary of her 1982 operational definitions is given. There are two excellent chapters, by Patterson and Spohn, on the contributions of neurosciences to the understanding of psychophysiology. Their review of the methodological advances in this complex research field attempts to link up-to-date findings with directions in the subclassification of schizophrenia. In another chapter, Linn endorses the view that supportive psychotherapy, with emphasis on relieving environmental stresses and encouraging the acceptance of realistic goals, has an important role in treatment. Information on maintenance medication and the issues of dosage, discontinuance, and relapse rates are reviewed by Linden *et al.* The development of the concept of expressed emotion and its application to studies of family interventions are summarised in a clear review by Leff. Social skills training aimed at improving interpersonal relationships and promoting community adjustment is described by Falloon.

Most of the papers emphasise a holistic approach to the understanding and management of schizophrenia, and, as review articles, they are of a high standard. However, even allowing for the long gestation period preceding publication, some of the information is dated and few references go beyond the early 1980s.

In spite of some outstanding contributions, this is not a book to be strongly recommended to the *Journal's* readers.

MOUNIR EKDAWI, *Consultant Psychiatrist, Netherne Rehabilitation Service, Coulsdon, Surrey*

Fantasy, Myth, and Reality: Essays in Honor of Jacob A. Arlow, MD. Edited by HAROLD P. BLUME, YALE KRAMER, ARLENE K. RICHARDS and ARNOLD D. RICHARDS. Madison: International University Press. 1988. 538 pp. $55.00.

This book is a collection of papers written in honour of Jacob Arlow, an eminent North American psychoanalyst. His particular interests were in unconscious fantasy, mythology, 'modernisation' of the structural theory, and matters of psychoanalytic technique. The contributors are training analysts, professors of psychiatry or psychology and others. The writings are of the highest standard and should appeal particularly to those working within the framework of ego-psychology. There are 28 papers, all of which take as their starting point one or other of Arlow's areas of interest.

I found a number of the papers of interest, mainly in the clinical area; three particularly. The paper titled "Self-mutilation and father-daughter incest" describes a young woman's conflicts over an incestuous relationship, which are acted out in self-mutilating behaviour. "Dynamic aspects of homosexual cruising" gives a vivid and lively account of the analysis of a bisexual patient. "Unconscious fantasies: the hidden agenda in treatment" illustrates most clearly just why unconscious fantasy is so important and needs to become explicit in therapy.

TOM MURPHY, *Consultant Psychotherapist, Royal Edinburgh Hospital*

Melatonin: Clinical Perspectives. Edited by ANDREW MILES, DAVID R. S. PHILBRICK and CHRISTOPHER THOMPSON. Oxford: Oxford Medical Publications. 1988. 288 pp. £40.00.

This book is unusual in that it's title belies it's actual usefulness in practice. All the psychiatrist contributors, except one, conclude that there is little evidence for the involvement of melatonin in the major psychiatric disorders. It is also unusually catholic in approach, including chapters on ageing, reproduction, sleep, seasonal affective disorder, thyroid disease, and a host of other topics. In fact, only four of the fourteen chapters deal directly with issues of interest to psychiatrists.

This book is not for the fainthearted. One of the difficulties is the detail with which the major experiments leading to the current "state of the art" are described. Many of these are of relevance to veterinary rather than human clinical practice. The style of writing varies enormously; some of the chapters, mainly those dealing with non-psychiatric disturbances, are somewhat turgid, while others are more easily comprehended. The chapter on 'Melatonin and the human circadian rhythm' is easily absorbed and makes the reader aware of the complexity of this intriguing hormone. The chapters on seasonal affective disorder and schizophrenia are also models of clarity and succinctness. The authors themselves are obviously perspicacious in nature and frequently pose questions of their own, thereby pointing out directions for future research. The book is also well referenced.

It is striking that this book should draw so much from so little, since in the authors' final words, "No investigators have yet been able to positively identify a clinical syndrome clearly caused by disordered pineal function." Inevitably, the financially constrained library will not consider this book, nor will general psychiatrists derive much by way of clinical acumen from it. However, those who have an interest in neuropsychiatry will find it engrossing, but will in a few years be forced to dig into their pockets again for the second edition if the pace of research into this hormone continues as it has started.

PATRICIA CASEY, *Senior Lecturer, Department of Psychiatry, University College, Cork, Ireland*

Selective 5-HT Reuptake Inhibitors: Novel or Commonplace Agents? Edited by M. GASTPAR and J. S. WAKELIN. Basle: Karger. 1988. 108 pp. £44.60.

The new generation of selective inhibitors of 5-HT uptake represent a significant addition to our therapeutic armamentarium, and a clinically-orientated book on the subject would be a useful addition to any psychiatric library. Unfortunately, this book does not provide what the clinician needs.

It does contain one excellent review by Bech of the available evidence on the therapeutic efficacy of these drugs. He makes the point that although there are some studies in which the new drugs are inferior to the reference compounds, there are none in which they are superior in efficacy. He concludes from this that the case for therapeutic equivalence of new and old drugs has yet to be established. The efficacy of the new ones is not in doubt – the question is whether they are worth the price.

The other jewel in this collection of papers is an account of the action of the drugs on the electrophysiology of 5-HT neurones. Two adaptive processes are described which lead to increased 5-HT neurotransmission. Down-regulation at cell body 5-HT autoreceptors keeps the cells firing in the presence of high 5-HT levels, and down-regulation at 5-HT autoreceptors on nerve terminals keeps the terminals releasing 5-HT even in the presence of high intrasynaptic 5-HT concentration.

Although useful in some ways, the other chapters do not provide the information that a clinician needs to evaluate this new class of drugs. The index makes no reference to the principal side-effects of nausea, vomiting, diarrhoea, and headache; nor does the book give any clues as to the problems these drugs have had getting onto the market. No mention is made of the safety of these drugs in overdose and in patients with cardiac illness. I am using them in these situations because, logically, they should be safe, but data on these points should be presented and discussed. The drugs are not only selective inhibitors of 5-HT, they are also extremely potent. Consequently, their combination with lithium or MAOIs might produce unwanted effects. I have seen no problems with combining one of these drugs with lithium and there is a small literature on the subject of which clinicians should be aware.

Maybe the book is just a bit premature, and in a few years time someone will be able to edit the book we need on 5-HT uptake inhibitors.

STUART CHECKLEY, *Consultant Psychiatrist, Maudsley Hospital, London*

Illusion and Spontaneity in Psychoanalysis. By JOHN KLAUBER *ET AL.* London: Free Association Books. 1987. 197 pp. £27.50 (hb), £9.95 (pb).

This book contains four of Klauber's lectures prepared as a part of a series for the Freud Memorial Visiting Professorship at University College, London, which sadly he never delivered because of his untimely death. Together with these are three essays by former analysands of Klauber (Neville Symington, Roger Kennedy, and Patrick Casement) and three essays by close European colleagues (Nicole Berry, David Widlöcher, and Helmut Thomä), written in appreciation of the thoughts of Klauber.

The book, as its title suggests, is devoted to those two vital themes of thought within the Independent Group of British Psychoanalysis, illusion and spontaneity. To those unfamiliar with Klauber's earlier work, the most helpful essay is that by Symington, who writes more clearly that anyone else in this volume on Klauber. Klauber himself is more reticent in his style, and comes across as overcautious, perhaps because of his anticipation of a more general audience. He is concerned that the reality of the psychoanalyst's personality and private values should be taken more into account than is usual when considering the therapeutic interactions of psychoanalysis. He sees countertransference as including more than merely the psychoanalyst's responses to his patient's transferences. The capacity of the psychoanalyst and his patient to sustain and also to survive the illusion of the transference is at the heart of his concept of the therapeutic process in psychoanalysis. It is not so clear how he sees the analysts's capacity to be spontaneous in this process. Here I found the French psychoanalyst Berry, writing about the termination of an analysis, alive and illuminating. The contributions of Widlöcher and Thomä seem ponderous by comparison.

The problem of illusion in psychoanalysis is much broader than this book implies. It is surprising that such a text should contain so little reference to transitional phenomena, let alone the enormous difficulties that some patients have in arriving at a capacity for illusion when they enter a psychoanalysis.

PETER SHOENBERG, *Consultant Psychotherapist, Joint Department of Psychotherapy, University College Hospital and Middlesex Hospital, London*

Aggression and War: Their Biological and Social Bases. Edited by JO GROEBEL and ROBERT A. HINDE. Cambridge: Cambridge University Press. 1989. 237 pp. £25.00 (hb), £8.95 (pb).

In a world that appears to be saturated with the rhetoric of violence, my approach to this book was one of enthusiasm in a search for some clear-headed perspectives. I had another reason for hoped-for enlightenment: a good deal of my work in retirement is with staff who supervise those who have committed serious acts of violence and in whom there is considered to be a propensity for them to do so again. For both these reasons I found this book, edited by two distinguished academics, an enlightening and enjoyable read. Its origins are in work that was done to formulate a short statement on violence. The statement was produced in Seville in 1986, and was signed by 20 experts from 12 countries.

The editors have drawn together a group of well-known workers from a variety of disciplines – animal ethology, zoology, psychology, physiology, biology, genetics, education, and politics. Their contributions are grouped into six sections: 'Agression: the reality and the myth', 'Biological mechanisms in the individual', 'Individual aggression and pre-social alternatives', 'Communication and group processes', 'The macro level: societies and nations' (an extrapolation to the study of warfare), and a concluding section. Each section is prefaced by a carefully written editorial making well-articulated links between the various expositions. In addition to these editorials, it is clear that the editors have put in a great deal of work to facilitate a uniform and refreshingly jargon-free presentation. Inevitably, there are minor weaknesses; there are areas of overlap and repetition, but in the main these are helpfully reinforcing rather than irritating. A little more editorial oversight of the citation of references and guidance for further reading would have facilitated a more consistent approach.

I imagine that readers of this *Journal* will find the chapters on biological, genetic, physiological, and social learning factors the most relevant to their day-to-day work. However, the contents as a whole afford a most useful guide to an area which is more full of myths than facts. In this connection the editors rightly state that, "In the long run, it is the myths that are largely responsible for both individual aggression and war". This book goes a long way towards helping dispel some of them.

HERSCHEL PRINS, *Lecturer on Social Aspects of Forensic Psychiatry*

Cognitive Behavioural Interviewing for Adult Disorders: A Practical Handbook. By PETER H. WILSON, SUSAN H. SPENCE and DAVID J. KAVANAGH. London: Routledge. 1989. 247 pp. £10.95 (pb), £25.00 (hb).

This book aims to be a practical guide to help student clinicians carry out the initial interview in the cognitive-behavioural treatment of psychological disorders typically seen in adult out-patients. Eight common psychological problems have been selected to illustrate the kinds of questions that need to be asked about these disorders before they can be appropriately and successfully treated: fear and anxiety; depression; obesity; interpersonal problems; sexual dysfunction; insomnia; headaches; and substance abuse. Surprisingly, how the trainee clinician decides whether any of these constitutes the patient's major reason for seeking help is seen as unproblematic and is not covered.

A chapter is devoted to each of these problems, each consisting of four main sections which, with few exceptions, follow the same format and sequence. The main features generally believed to characterise the disorder are discussed in the first section. This is done largely in terms of DSM–III and DSM–III–R where this is felt to be appropriate. The introductory section also provides a detailed and well-referenced summary of the current knowledge about the causes of the problem. The second section contains a large number of examples of the kinds of questions which may be asked to find out about such aspects as the history, the severity, and the factors associated with changes in the nature of the disorder. Some of the specific measures which have been developed to assess these disorders are outlined in the third section. The relevance and necessity of these measures for the cognitive-behavioural treatment of these problems, however, is never made clear. The final section is generally no longer than a page or two, and provides an all-too-brief indication of some of the techniques which may be used to treat these problems.

This book provides a useful and up-to-date summary of information about the aetiology and assessment of these specific problems. However, posing questions without adequately discussing the use to which the answers will be put is like asking for directions while not knowing where one is going. Consequently, the reader who is unfamiliar with cognitive-behavioural modes of treatment will find it difficult to judge the relevance and value of the questions provided.

DUNCAN CRAMER, *Lecturer in Social Psychology, Department of Social Sciences, Loughborough University of Technology, Loughborough*

Between Psychology and Psychotherapy: A Poetics of Experience. By MILLER MAIR. London: Routledge. 1989. 292 pp. £25.00 (hb), £9.95 (pb).

This book is an attempt to develop ideas for the project of keeping the personal relationship in view in psychological treatments, by balancing the reductionistic model of psychology as an applied science. It is structured like a sandwich, with the beginning and end containing collections of essays and lectures, and an intensely personal middle section of the author's own thoughts and feelings in poetry form, written over a ten-year period.

His declared interest is in developing an "intimate" rather than "distant" knowledge which can be used in the relationship with the patient/client, so that there can be "imaginative participation" between the two. He is not the first person to do this, and parts of the book reminded me of Robert Hobson's *Forms of Feeling*, to which he refers.

There is a good section on the use of metaphor as a tool for dynamic understanding, illustrated with case material.

I began this book with some trepidation, as I tend to feel suspicious of words like 'poetics'. However, because of the very personal way the book was written and the structure, I found myself actively caught up in the author's own struggle to develop and communicate his ideas, and in many ways found this matching of form and content one of the most satisfying aspects of the book. The atmosphere of struggle to capture the meaning of emotional experiences and how they are communicated is made vivid and exciting, and this way fulfils the author's hope of providing a counterbalance to an investigative mode, which by dissection often seems to destroy the subject of study.

This is not a textbook in the conventional sense, but the author, by staying with his own personal thoughts and feelings, vividly conveys the importance of the therapist's participation in the therapeutic process.

I would recommend this book to anyone who feels in need of refreshment in the battle to protect psychotherapeutic work with patients which does not fit into treatment "packages", so attractive to management and technocrats who, to quote the author, "believe we are simpler than we know we are".

RACHEL LEHEUP, *Consultant Child and Adolescent Psychiatrist, Nottingham*

Concise Guide to Clinical Psychiatry. By Steven L. Dubovsky. Washington: American Psychiatric Press (distributed in the UK by CUP). 1989. 198 pp. £9.95.

This slim (6″ × 4″) volume would easily slip into the side pocket of a suit or the rear pocket of designer jeans. This is not its only merit, and I was pleasantly surprised to have learned much from the author's commonsense clinical approach. It is one of the American Psychiatric Association's *Concise Guide* publications, and is intended for medical students and young psychiatrists in training, working mainly in the general hospital or outpatient setting. I think it would be a useful introduction for general practitioners in this country, since it is replete with commonsense and clinically useful ideas. The format relies heavily on DSM–III classifications; depression, anxiety, organic mental disorders, substance abuse, and psychoses are covered. Some of the chapters are rudimentary, but I found the sections on sleep disorders and somatoform (hypochondriacal) disorders particularly informative. The book is pervaded by a sense of optimism and certainty which those of a philosophical or cynical disposition might find simplistic or even offensive. Nevertheless, its author's sound clinical acumen and confident approach makes a welcome change from the sometimes hypertheoretical and critical approach of many books written on this side of the Atlantic.

I enjoyed this book very much and would recommend it highly to medical students and general practitioners in this country. I look forward to reading other books in this series.

Eric Shur, *Consultant Psychiatrist, Westminster and Gordon Hospitals and Honorary Senior Lecturer, Department of Psychiatry, Charing Cross and Westminster Medical School, London*

Somatic Therapies in Psychiatry. By Laurence B. Guttmacher. Cambridge: Cambridge University Press. 1989. 164 pp. £9.95.

This little book will be a godsend to psychopharmacotherapists, but may be less enthusiastically received by psychiatric nosologists. There are sections on antipsychotics, antidepressants, agents for bipolar disorders, drugs for anxiety and insomnia, and geriatric psychopharmacology. There is a review of ECT, and the controversial issue of informed consent is firmly addressed. Two model consent forms – one long and the other brief – are appended. The waxings and wanings of the popularity of ECT are charted, and the film *One Flew Over the Cuckoo's Nest* merits a dishonourable mention. Drugs are dealt with comprehensively, but some recent somatic treatments are neglected, like the bright light therapy for the melancholy experienced in the dark winter months or the latitudes of the high Arctic.

The risks of combining ECT, lithium and antipsychotic drugs are discussed, as are the considerations involved in choosing between lithium and carbemazepine in the treatment of mania. The author rightly condemns the uncritical prescription of benzodiazepines without considering non-drug alternatives. The book is so up-to-date that the piece on buspirone had appeared before the drug trial evidence of its efficacy.

Up to this point I mostly applaud the sentiments expressed, but, I suspect in company with many European psychiatrists, I was unhappy with the view that there was little merit in distinguishing between endogenous and non-endogenous depression, a rejection of the wisdom of the past in line with other recent pragmatic US views on classification, e.g. DSM–III, which derives more from committee consensus than from clinical evidence.

However, to dwell on these discordances is to be ungenerous. The book is strong on the drug treatment of schizophrenia and affective illness, and the section on lithium is admirable. There are also two warnings to be heeded by practising clinicians: the risk of Ebstein's malformation in pregnant women given lithium during the first trimester of pregnancy; and the hazards of anticholinergic toxicity linked with prescribing antidepressants to the elderly.

The book will help many practising clinical psychiatrists. The price will suit most pockets.

M. W. P. Carney, *Northwick Park Hospital and Clinical Research Centre, Harrow, Middlesex*

Frontiers in Neuroendocrinology. Volumes 9 and 10. Edited by Cuciano Martini and William F. Ganang. New York: Raven Press. 1986, 1988. 282 pp, 343 pp.

These are part of a well-respected series of reviews of recent advances in basic neuroendocrinology. They are very basic, and I struggled for a long while to find some clinical lesson from a chapter on the neuroendocrine system of the fruit fly. Volume 10 has more to offer, and includes an encyclopaedic review of the distribution of 38 neuropeptides in almost as many brain regions. The expression and regulation of genes for hormones is an area of importance and a mechanism for slowly acting negative feedback mechanisms; several chapters discuss this, in connection for example with the new hormone atrial natriuretic factor, and also POMC.

The series should be in every university library, but will not be read by many psychiatrists.

Stuart Checkley, *Consultant Psychiatrist, The Maudsley Hospital, London*

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REFERENCES

1. Johnson DAW and Malik NA; Acta Psychiat Scand 1975; *51*: 257-267.
2. Pinto R, Bannerjee A and Ghosh N; Acta Psychiat Scand 1979; *60*: 313-322.
3. Hamilton M, Card IR, Wallis GG and Mahmoud MR; Psychopharmacol 1979; *64*: 225-229.

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